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A

TEXT-BOOK
OF
PHYSIOLOGY,

NORMAL AND PATHOLOGICAL.

FOR STUDENTS AND PRACTITIONERS OF MEDICINE.

BY

WINFIELD S. HALL, PH.D. (Leipzig), M.D. (Leipzig),
PROFESSOR OF PHYSIOLOGY, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO; MEMBER
OF THE AMERICAN PHYSIOLOGICAL SOCIETY; CHAIRMAN OF THE SECTION OF PATHOLOGY
AND PHYSIOLOGY, AMERICAN MEDICAL ASSOCIATION 1904-5; FELLOW OF THE
AMERICAN ACADEMY OF MEDICINE; MEMBER OF AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, ETC., ETC.

SECOND EDITION, REVISED AND ENLARGED.

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DORNAN, PRINTER

TO

HIS TEACHER

CARL LUDWIG

THIS BRIEF WORK

IS

DEDICATED

IN

REVERENCE AND GRATITUDE

BY

THE AUTHOR.

96385

PREFACE TO SECOND EDITION.

THE kind reception and favorable criticism given to the first edition of this work by medical educators and by practitioners appear to have justified the author's hope that it would supply a well-defined need.

The second edition, herewith presented, has been carefully revised and is much enlarged. The modifications are such as to make the work more especially adapted to the needs of two classes—medical students and medical practitioners. The mathematic and chemical formulæ have been simplified and condensed or, in some cases, omitted, while those portions which deal with the application of physiology to clinical medicine have been much amplified.

The most notable additions to the work are the sub-chapters on Pathologic Physiology. It is becoming apparent to medical educators that to master normal physiology alone without applying its laws to the symptomatology of disease is to miss a large part of the service which physiology should render, just as the mastery of structural or morphologic pathology without an understanding of the modification which structural changes induce in the functions, implies the loss of a large part of the advantage which the study of pathology should give to the student and practitioner of medicine. The author has attempted to cover this most important field. It was thought wise to use somewhat different methods in presenting the pathologic physiology of different fields of physiology. The sub-chapters on Pathologic Physiology occur at the ends of the following chapters: Circulation and Blood, Respiration, Digestion, Metabolism and Excretion. In the chapters on the Special Senses and the Central Nervous System it seemed advantageous to discuss their pathologic physiology within the body of the chapter.

Without assistance from clinicians and pathologists the preparation of the sections on Pathologic Physiology would have been quite impossible. The author takes this opportunity to acknowledge his obligations to his colleagues, designating the contribution of each:

Charles Louis Mix, A.M., M.D., Professor of Physical Diagnosis, formerly of Neurology and Clinical Neurology. *Physiology of the Nervous System, Normal and Pathologic.*

Gottfried Koehler, Ph.G., M.D., Instructor in Clinical Pathology. *Pathologic Physiology of the Digestive System.*

Charles J. Kurtz, A.M., M.D., Instructor in Physiology (Hæmatology). *Pathologic Physiology of the Blood.*

Theron J. Kinnear, A.B., M.D., Assistant in Physiology. *Pathologic Physiology of the Circulatory and of the Respiratory Systems.*

Jacques F. Hultgen, M.D., Research Fellow in Pathology. *Pathologic Physiology of Metabolism and of Excretion.*

The author wishes also to acknowledge his obligations to Dr. Henry Crew, Professor of Physics, Northwestern University; to Dr. William A. Locy, Professor of Biology, Northwestern University; and to Dr. John H. Long, Professor of Chemistry, Northwestern University Medical School, for many valuable suggestions and criticisms in their respective fields.

The author takes this opportunity to thank his publishers for their cordial support and assistance throughout, and more particularly in the extensive revisions of the illustrations. Besides the valuable illustrations contributed by Professor Piersol, Professor E. B. Wilson, and Professor Walker—acknowledged in the Preface to the First Edition—the author acknowledges the engravings from Szymonowicz's *Histology.*

The figures illustrating the innervation of the circulatory, respiratory, and digestive systems were drawn by Claude H. Barlow, Demonstrator in Histology, as was also the ingenious figure of the Sympathetic Nervous System, which is a valuable and original contribution.

W S H.

Chicago, 1905.

PREFACE TO FIRST EDITION.

PHYSIOLOGY is an experimental and superstructural science occupying a field quite as definite as Anatomy, Chemistry, and Physics, the three foundations on which it is built. Though all physiologists impress these facts in their teaching, no volume has hitherto been based on the advantages of presenting the subject concretely within its own proper boundaries, and in its instructive connections with the sciences whence it is derived.

In approaching Physiology from this standpoint the author has summarized in the Introduction those principles of Physics and Chemistry which have a general application, and has prefixed to each chapter an abstract of the facts drawn from all three of the basic sciences which are to be applied in the succeeding text. This method possesses the obvious teaching value of confining the subject-matter of each chapter strictly to Physiology and presenting it in logical relations.

The plan of the work adapts it to the needs of several classes of readers. Medical students will, it is hoped, find a clearly defined exposition of Physiology proper, its relevant facts from Chemistry, Physics, and Morphology, and accompanying outlines enabling them to arrange their knowledge in an orderly and logical manner. Students in literary or scientific institutions who are preparing for the study of medicine or of physiology as a specialty, will find the method of the book equally adapted to their needs, inasmuch as the general and special introductions review matter which has been the subject of detailed study in the laboratories of Physics, Chemistry, and Biology, and which forms the basis of Physiology.

The same reasons render the method of the book convenient for the practitioner. The style is as brief and concise as compatible with the needs of students, and space has thereby been gained for the inclusion of clinical applications of physiologic facts and principles.

Readers interested in physiologic chemistry will find the structural formulas and reactions of the complex bodies involved in Physiology worked out in as much detail as the present status of chemistry will allow. The newer literature of this subject is noted in references.

Though the volume embodies original work on the part of the author, free use has been made of the great heritage of physiologic knowledge without which no adequate presentation of the subject would be possible.

The author wishes to express here his obligations to Professor Piersol for the use of many of his excellent histologic illustrations; to Professor E. B. Wilson for the use of several fine figures from his work on *The Cell in Development and Inheritance;* and to Professor Waller for several valuable engravings from his *Text-book of Physiology.* Several authors have contributed one or two figures each. Many have been taken from my *Laboratory Guide in Physiology.*

WINFIELD S. HALL.

CHICAGO, 1899.

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PHYSIOLOGY.

INTRODUCTION.

A. THE SCOPE OF PHYSIOLOGY AND THE PROBLEMS WITH WHICH IT DEALS.

1. DEFINITIONS.

PHYSIOLOGY *treats of the functions of different cells, tissues, and organs of living organisms.* Living organisms are divided into plant and animal kingdoms; so there is *Plant Physiology* and *Animal Physiology.* It has been customary to subdivide the latter into *Comparative Physiology,* treating of the ways in which the different functions—digestion, circulation, etc.—are performed in the different classes of animals, and *Human Physiology,* treating of the special physiology of man. Another subdivision of the subject is into *General Physiology,* treating of the general functions of cells and tissues, and *Special Physiology,* treating of the special functions of organs and systems of organs.

Defined in more general terms—*Physiology is the science of the phenomena of living nature.* Reduced to its final elements, a natural phenomenon always involves matter and energy. A general knowledge of the properties of matter and of energy is of great importance to him who would study the phenomena of life.

2. MATTER.

All things in the universe which affect our senses are called matter. The three most characteristic general properties of matter are inertia, gravitation, and elasticity. The amount of matter which a body contains is often called its *mass.* The mass of one body may be compared with that of another by means of a balance. Physicists, chemists, and astronomers find it a necessity to assume the existence of a very tenuous form of matter which is called "*the ether.*"

It is supposed to fill all space not actually occupied by ordinary matter, and to transmit the sun's heat and light to us through space. This form of matter cannot be weighed in a balance.

Physiology is concerned principally with ordinary matter.

A limited portion of ordinary matter is called a *body*. A body which is small when compared with the other quantities involved is called a *particle*.

Bodies the relative positions of whose parts admit of no change whatever are said to be *rigid*. No perfectly rigid bodies are known. Bodies which can be altered, either in size or shape, are called *elastic*. If a body has both elasticity of size and shape it is said to be *solid;* if, however, it possesses elasticity of size and not of shape, it is known as a *fluid*. There are two kinds of fluids: (1) those which fill any vessel however large, and (2) those which when placed in a large vessel remain at the bottom of it and only partly fill it, even when the pressure is removed. The former are called *gases;* the latter, *liquids*. This classification may be put into tabular form as follows:

Bodies . . . . .
- Rigid—not known in nature.
- Elastic
  - Solids.
  - Fluids
    - Gases.
    - Liquids.

3. ENERGY.

Energy is defined as capacity to do work, and is, therefore, measured in the same units as work. A mechanical system may possess energy either by virtue of the relative position of its parts or by virtue of the relative speed of its parts. The former is called *potential energy;* the latter is called *kinetic energy*. There are many forms of energy which for convenience we put in classes by themselves. Among these are the energy due to the temperature of a body, the energy due to the electric condition of a body, the energy due to the chemical composition of a body, etc.

1. **The Transformation of Energy.**—The various forms of energy mentioned above are transformed with more or less ease one into another. If one hold an object in an elevated position, and release it, it falls to a position of equilibrium. The kinetic energy of the mass disappears as such, but reappears as heat. The energy of mass or molar motion is thus transformed into the energy of heat. The heat may be so great that the vibrations appeal not only to our temperature sense as heat, but also to our eyes as light. Still another form, in which energy may appear, is electric energy.

Another common form of energy, easily transformed into the form of heat, light, or electricity, is chemical energy. By virtue of molecular attraction every molecule of matter is attracted by every other molecule irrespective of the kind of matter; but, by virtue of a peculiar affinity between atoms of certain different kinds of matter, these atoms are drawn into new and most intimate contact, manifested by heat or light or electricity, and resulting in a new combination of matter, having physical properties different from those of either constituent. This kind of energy, and its transformation forms, are of the most fundamental importance to physiology.

Matter may be transformed, but not destroyed; in the same way energy may be dissipated, but not destroyed. This great fact was discovered and demonstrated principally by Helmholtz and Joule, and may be looked upon as the most important advance of physical science during the nineteenth century. It is called the law of the conservation of energy.

2. **Law of the Conservation of Energy.**—Ganot expresses this law as follows: "The total amount of energy possessed by any system of bodies (*e. g.*, the solar system) is unaltered by any transformations arising from the action of one part of the system upon another, and can only be increased or diminished by effects produced upon the system by external agents."

The unit of mechanical energy is the *erg*, which is the amount of work done when a force of 1 dyne is exerted through a distance of 1 centimetre. The unit of heat energy, called the *calorie* or gram-calorie, is that amount of heat required to raise 1 gram of water 1 degree of temperature. If it is required to reduce units of mechanical energy to units of heat, one has only to remember that experiment has proven that 425.5 grams, falling through a distance of 1 metre, would by impact generate enough heat to raise the temperature of 1 gram of water 1° C. The number of ergs in a calorie (very approximately 42,000,000) is known as the mechanical equivalent of heat. The principles involved in the transformation of energy, and the conservation of energy, are fundamental, and we shall presently see their inestimable importance in any clear conception of the phenomena of living nature. All natural phenomena involve matter and energy.

4. LIVING MATTER vs. LIFELESS MATTER.

The phenomena of living nature differ from those of lifeless nature simply in the matter or in the energy involved. We are at once brought face to face with the most difficult problem of Physiology —the abstract differentiation between living and lifeless matter.

Let us approach this subject by an enumeration of the kinds of matter of which living beings are composed. It was formerly sup-

posed that an analysis of the animal body would reveal chemical
elements peculiar to living bodies. Chemistry has, however, estab-
lished no fact more thoroughly than that the animal or plant body
72 contains no new kinds of matter. Analysis shows the presence of
13.5 carbon, hydrogen, nitrogen, oxygen, sulphur, phosphorus, chlorine,
and of sodium, potassium, calcium, magnesium, iron—occasionally
9. traces of silicon, manganese, fluorine, lithium, bromine, and iodine
are found. These are the most common elements in the surface of
2.5 the earth.

After finding that living nature differs in no way from non-living
1.3 nature as to the kinds of matter involved, the physiologist turned
to the investigation of the kinds and forms of energy, expecting to
1.15 find associated with life a new energy. Until quite recently, most
1. physiologists, since the time of Johannes Müller, have believed
that the energy manifested in living nature is identical with that
.05 manifested in non-living nature, and, further, that it obeys the same
laws of transformation in living as in lifeless bodies. This belief
.026 was based upon observation in a large number of physiological
phenomena. For example, it has been demonstrated that the heat and mechanical energy which an animal may expend is exactly equivalent to the potential energy represented by the food which the animal absorbs.

There remain, however, many unsolved problems regarding the energy involved in absorption, secretion, and excretion. The more these problems are studied, the clearer seems to be the indication that energy may undergo, in the animal or plant organism, a transformation not observed outside of living organisms. Along with this indication comes repeated and indubitable proof that, whatever transformations energy may undergo within the living organism, the quantity of energy that leaves the organism, dissipated into space as heat, is exactly equal to the quantity that enters the organism as potential energy. Whatever may be said about vital energy, it is certain that it is not to be supposed that any new energy is created by living organisms.

In discussing the matter involved in living organisms, the elements which occur in living bodies were enumerated, but the study of the combination of these atomic elements into molecules was omitted. In lifeless nature we find as typical molecules, H_2O, CO_2, $CaCO_3$, $MgCO_3$, NaCl, $CaSO_4$, KNO_3, Fe_2O_3, PbS, etc.

These typical compounds, which make up a large proportion of the earth's crust, are composed each of three to six atoms of two to three kinds of matter. There are, however, in the realm of inorganic nature, some very large and complex molecules, *e. g.*: crystalline ammonioferric alum $Fe_2(SO_4)_3(NH_4)_2SO_4 + 24H_2O$. This complex molecule contains 104 atoms, and has 962 times the weight of H. One of the simplest molecules met among the products of life is the glucose molecule ($C_6H_{12}O_6$), whose 24 atoms weigh 180 times as much as an atom of hydrogen. Egg albumen was given by Hofmeister the formula: $C_{204}H_{322}N_{52}O_{66}S_2$; its 646 atoms weigh 4618 times as much as hydrogen. Zinoffsky determined the formula for the hæmoglobin of the horse's blood corpuscle to be: $C_{712}H_{1130}N_{214}FeS_2O_{425}$. This prodigious molecule has 2304 atoms and a molecular weight of 16,710. Here we have struck the key-note of the difference between living and lifeless nature. *In its composition, living matter differs from lifeless matter not in the kind of material elements, but in the complexity of the combinations.* A similar course of reasoning, applied to the energy, would result in the conclusion that: *The energy involved in the phenomena of living nature differs from the energy involved in the phenomena of lifeless nature only in the complexity of the transformations.*

5. LIFE.

Having now determined the essential difference between living and lifeless nature as to the matter and energy, let us investigate the nature of life in the abstract. Compare a dead with a living organism; take, for example, a frog just dead. We observe a cessation of activity—*i. e.*, a cessation of manifest energy. The breathing movements cease, the heart ceases to beat, the animal ceases to take food; it becomes cold; in a few hours disintegration of the material begins. How shall we interpret this change? The activities which have ceased were the activities which adjusted the animal to its environment; built up its tissues from its food; and brought a continuous supply of oxygen to enter into combination with the tissues, and liberate the energies which were manifested in the phenomena of life. With the loss of life has been lost the energy necessary to adjust the internal needs of the body to the action of the environment. Herbert Spencer defines life as "*The continuous adjustment of internal relations to external relations.*" A concrete idea of the typical phenomena of life may best be gained from the observation of a living organism.

6. A LIVING ORGANISM.

Such an organism begins its life as a minute globule (cell) of sensitive, spontaneously moving matter (protoplasm). The original volume is always increased (growth) by addition of matter from within (intussusception). Having attained a certain maximum of volume (maturity) the organism retains essentially the same volume for a time (adult life), and finally divides into equal or unequal parts (reproduction), the parts divided off beginning again the cycle of life, reaching, at maturity, a form always resembling the parent organism in form and activity. During the whole period of life there are certain activities which are manifestations of energy, liberated within the organism through a process analogous to a combustion of tissue (respiration—destructive metabolism), which tissue is regenerated by the building up in the tissue (constructive metabolism) of elements or compounds taken in as food, dissolved (digestion), and carried to the wasted tissues (circulation). After growth is completed, and reproduction consummated, the wasting of the organism progresses faster than the regeneration (period of senility), and, finally, the internal relations (needs) fail to be adjusted to the external relations (conditions of environment), and the organism dies.

McKendrick (*General Physiology*, p. 31) gives the following valuable recapitulation of the essential characters of a living being:

(*a*) Molecular complexity; heterogeneity of parts, and chemical instability of the organic compounds forming it.
(*b*) Waste, and incessant repair of organic materials.
(*c*) The conversion of kinetic into potential energy, as the framework of the body is built up, or stores of reserve material are formed.
(*d*) Liberation of kinetic energy in various modes, and, in particular, as mechanical movement, heat and electricity.
(*e*) Organization, or the adaptation of certain parts of the body to particular functions.
(*f*) A regular evolution from origin to death.
(*g*) Origin from a parent, and the possibility of producing the elements of offspring.
(*h*) A power of variability and of adaptation to external conditions.

Physiology deals with the problem of NUTRITION; including *digestion*, *absorption*, *respiration*, *circulation*, *constructive* and *destructive metabolism*, *secretion*, and *excretion;* with the problems of MOTOR-SENSORY ACTIVITY, including the functions of the motor and nervous, and systems of the special senses; and, finally, with the problems of REPRODUCTION.

B. THE RELATION OF PHYSIOLOGY TO THE OTHER NATURAL SCIENCES.

- **THE NATURAL SCIENCES.**
  - **The Physical Sciences.**
    - *Chemistry.*
    - *Physics.*
    - *Astronomy.*
    - *Geology.*
  - **The Biologic Sciences.**
    - MORPHOLOGIC.
      - 1. *Anatomy.* Science of living forms.
        - Gross.
        - Minute.
          - Plant or Animal.
      - 2. *Paleontology.* Science of fossil forms.
        - Paleophytology.
        - Paleozoology.
    - PHYSIOLOGIC.
      - 1. *Physiology.* Science of functions of living organisms.
        - General.
        - Special.
          - Plant or Animal.
      - 2. *Psychology.* Science of psychic phenomena.
        - Comparative.
        - Human.
      - 3. *Pharmacology.* Science of the action of drugs.
        - Comparative.
        - Human.
    - MORPHOPHYSIOLOGIC.
      - 1. *Embryology.* Science of development of structures and functions.
        - Comparative.
        - Special.
          - Plant or Animal.
      - 2. *Pathology.* Science of diseased forms and functions.
        - Comparative.
        - General.
        - Special.
          - Plant or Animal.
      - 3. *Anthropology.* The Biology of Man
        - *a.* Physical Anthropology. The Animal, Homo.
        - *b.* Ethnology. Races of Homo sapiens.
        - *c.* Ethnography. Geographic distribution of the races.

C. THE DEVELOPMENT OF PHYSIOLOGY AS A SCIENCE.

HISTORIC REVIEW.

5th B.C.		Heracles and Empedocles (500 B.C.). Hippocrates (460 B.C.).			
4th B.C.	Antiquity.	Aristotle (384 B.C.).			
3d B.C.		Erasistratus (280 B.C.).			
2d B.C.					
1st B.C.					
A.D. I.	Early Christian Era.				
II.		—131 —200 } Galen.			
III.					
IV.					
V.					
VI.	Middle Ages.				
VII.					
VIII.					
IX.					
X.					
XI.	Dark Ages.				
XII.					
XIII.					
XIV.					
XV.		Paracelsus (1490).			
XVI.		Servetus (1511).			
XVII.	Modern Times.	Harvey.			
XVIII.		Haller.			
XIX.		Müller.	Zunst.	Halliburton.	Marey.
		Wöhler.	Kühne.	Weber.	Bernard.
		Liebig.	Hoppe-Seyler.	Brüke.	Hering *et al.*
		Voit.	Runge.	Ludwig.	
		Pflüger.	Hammersten.	Du Bois-Reymond.	

The first traces of vague physiologic conceptions are lost in the impenetrable darkness of prehistoric times. These vague conceptions find expression in mythology. In mythology there is no classification of knowledge: all knowledge being made to do homage to higher beings or deities, and this sum of human knowledge, as it existed in prehistoric times, must be looked upon as an indivisible whole from which, in the lapse of centuries, there gradually crystallized out: theology, philosophy, medicine, and natural science. In this mythologic period life was characterized by motion. Wind, water, fire, stars, sun, and moon were personified. In historic times the first traces of a science based upon observation was, curiously enough, metaphysics, or psychology.

The first attempt at biologic science laid as the corner-stone of its foundation the proposition, "The human being is dual—the physical and the psychic—the body and the soul," and rounded its dome with the theory of metempsychosis, or wandering of the soul. From India this system of philosophy gradually made its way through Egypt to Greece, where it was championed by Pythagoras.

It is remarkable that many of the philosophers of antiquity promulgated theories which are again, after a lapse of twenty-five centuries, forming the foundations of modern science. This is especially true of the theories regarding the origin and development of living nature.

Anaximander (620 B.C.) believed that man descended from animal-like progenitors, who originally lived in water. *Heracles* (500 B.C.) had a conception of the "Struggle for Existence." *Empedocles* (504 B.C.) believed that, in the realm of living nature, plants originated first, then lower animals, then higher animals, and finally man. He believed that the active factor in this development was the destruction, in their *struggle for existence*, of the animals unfavorably constructed, while those capable of survival propagated the species, and transmitted their favorable structures.

In the fifth century B.C. *Hippocrates* systematized medicine and wrote several volumes on the practice of medicine and midwifery. Hippocrates is looked upon as the *founder of the medical profession* —the "*Father of Medicine.*" His additions to knowledge were unimportant in morphology and physiology. His materia medica, therapy, and practice of medicine were incomparably superior to what had preceded, and stood unimpeached for six centuries.

In the fourth century B.C. *Aristotle*, the great observer of the phenomena of living nature, and the great collector of facts, laid the first enduring foundation for the *biologic sciences*, in consequence of which he is called the "*Father of Biology.*"

In the third century B.C. *Erasistratus*, of the Alexandrian school, was the first to attempt a philosophy of physical life—a theory of physiology. . He gave definite form to a theory which had its origin among the pupils of Plato, and which reached its highest development under Galen and his school. This theory is called the *Pneuma Theory,* and, according to it, the Pneuma zotikon—life-giving spirit, or breath of life—resided in the heart, while the Pneuma psychikon—the soul—resided in the brain. Medical science having taken definite and authoritative form under Hippocrates and physiology having been crystallized by the Pneuma theory of Erasistratus, there was a lapse of 400 years before there appeared the spirit who was destined to dominate the medical profession for more than thirteen centuries.

GALEN (130–200).

In the second century A.D. Galenus, a surgeon in the Roman army, made systematic dissections of the bodies of apes and other animals. Galen realized that medicine and surgery could not succeed unless based upon an exact knowledge of the structure of the body, and upon a knowledge of the vital functions; and, to the end last named, he performed vivisections upon apes and pigs, establishing the functions of the vagus, or pneumogastric nerve, and the intercostal nerves, and the effects of section of the spinal cord. After collecting a great mass of morphologic and physiologic knowledge he founded a *system of medicine.* His system of physiology was based upon the Pneuma theory, which, briefly expressed, was: *Pneuma psychikon*—the soul—resided in the brain and nerves, and presented the psychic phenomena, thought, sensation, and voluntary motion; *Pneuma zotikon*—life-giving spirit, or breath of life—entered the body through the lungs, resided in the heart, and expressed itself in heart-beat, pulse, and bodily warmth; while the *Pneuma physikon* resided in the abdomen, and is manifested in the functions of nutrition, growth, secretion, and reproduction. No subsequent Roman even approached the colossal work of Galen; so it is easy to understand that, after the fall of Rome, his was the only authority recognized until the new birth—the Renaissance—of art, literature, philosophy, religion, and science, in the fifteenth and sixteenth centuries. If, in all those thirteen centuries, any man doubted the statements or theories of Galen, he did not publish it, for Galen's authority was held to be unimpeachable. The first recorded combatant of Galen was *Paracelsus* (1493 A.D.). Though he founded an untenable theosophistic philosophy, the simple fact of his calling in question Galen's theories set the scientific world thinking. The feature of his system was, Unity in Nature; Nature a macrocosmus, and Man a microcosmus. Early in the sixteenth century *Vesalius, Eustachio,* and *Falloppius,* through dissection, extended the knowledge of anatomy; while *Servetus* disproved Galen's statement that the blood goes directly from the right heart to the left heart, and *Argentieri* contended that the blood nourished the tissues of the body. These advances prepared the way for the next great light in the Renaissance of physiologic science.

HARVEY (1578–1659).

This great experimenter and observer was taught by his predecessors that the blood was in motion within the arteries and veins, and that the heart movements were the cause of this motion, but it remained for him to demonstrate that the arteries and veins were connected by smaller vessels (though, through lack of a microscope, he never saw them), and that the blood circulated within a closed system of tubes from the left heart through the arteries and capillaries, and back through veins to the right heart, thence to the lungs, and completed the circuit by entering the left heart.

Next to this great triumph stands that noble proposition, first formulated by Harvey, "*Omne vivum ex ovo.*" The history of this proposition is most interesting. Twice it has been refuted, and twice the fallacies of the refutation have been demonstrated. Established at first on an observation of higher plants and animals, it was combated by the early microscopists, who found, in their nutrient infusions, a rapid development of infusorian life with no discoverable eggs or germs. A century later Treviranus proved the fallacy of this "*Spontaneous Generation*" theory through the discovery of the real method of reproduction of these organisms; so the theory that "*all life is from an egg*" had stood its first assault. The improvement of the microscope, however, revealed the microbe. Nutrient fluids were seen to be soon swarming with life; the *Spontaneous Generation* theory was again revived, Harvey's theory again combated; Pasteur has, however, in recent times, with his more exact instruments and methods, established, experimentally and conclusively, the verity of Harvey's proposition, "*All life is from an egg.*"

The microscope has been mentioned. It was in the latter part of the seventeenth century that Van Dyke and Leeuwenhoek invented the compound microscope, and *Leeuwenhoek*, with *Malpighius* and *Schwammerdamm*, made rapid strides in histologic research. Up to the beginning of the eighteenth century, physiology had not been a separate and independent science.

HALLER (1708–1777).

It was Haller who, by his power of systematizing and generalizing, collected the facts peculiarly physiologic, and constructed them into his renowned work, *Elements of the Physiology of the Human*

Body. But Haller was, unfortunately, a philosopher rather than a philosophic investigator. He promulgated two theories which have had a retarding effect on physiology, viz., *The Preformation Theory* and the *Theory of Vital Energy*. According to the first theory *the form of the organism existed in the egg*, and embryologic development was simply *increase in size*; while, according to the second theory, the *Energy of Life* is peculiar to life—i. e., not transformable from physical and chemical energy, and for that reason called *Vital Energy*. This theory of a peculiar Vital Energy has retained a most tenacious hold on Physiology, and only through the combined efforts of a galaxy of experimenters in the first three-fourths of this century has the theory that "the energy manifested in the phenomena of life is peculiar to life" been abandoned. For a time it was hoped that all of the phenomena could be accounted for in the usual transformation forms of energy. More exact and extended recent experimentation makes it evident that there is a transformation form of energy peculiar to life. The living organism is not believed to be able to make energy, but simply to give it a new and unexpected form under certain circumstances. It is important to note, in this connection, that this newly discovered form of energy obeys, with the other forms, the law of the conservation of energy.

At the end of the eighteenth century *Priestley* and *Lavoisier* discovered *oxygen*. *Girtanner* demonstrated that it is this constituent of the atmosphere which, in the lungs, effects the change between venous and arterial blood.

JOHANNES MÜLLER (1801-1858).

The spirit which inspired and dominated physiologic investigation during the first half of this century was Johannes Müller. Though he believed in a special Vital Energy, he believed that it followed implicitly the laws of energy in physics and chemistry, and set about, with physical and chemical methods, to investigate the phenomena of living nature. Johannes Müller was an indefatigable worker, an accurate and exact observer, a broad and judicious generalizer, and a profound philosopher. He was master of the whole field of Morphology and Physiology as it existed at the beginning of this century. He founded the new sciences of *Comparative Physiology* and *Physiologic Psychology*, and laid for modern experimental physiology the broad and deep foundations which have sustained the great superstructure erected by his pupils and successors during the last half century. Soon after his death physiology was divided into *chemical* and *physical* physiology. The physiologic chemists of the nineteenth century are Wöhler and Liebig, Voit, Pflüger and Zuntz, Kuhne, Hoppe-Seyler, Hammarsten, Kossel, Hofmeister, Bunge, and Halliburton.

The investigators in the field of physical physiology are, first of all, Ludwig, Weber, Du Bois-Reymond, and Brücke; then Marey, Claude Bernard, Helmholtz, Hering, Hitzig, Goltz, Fick and others. Inasmuch as frequent reference must be made to these men during the course of our study, a detailed account of each man will not be entered upon here.

The great discoveries of the nineteenth century, which have been of fundamental importance to physiology, are: (1) the *Law* of the *Conservation* of *Energy;* (2) the *discovery* of the *cellular structure* of *animal organisms;* (3) the discovery of the genealogy of the organic world—*i. e., the establishment of the Evolution Theory.*

These three great principles have already been of inestimable value to physiology, but their service has only just begun.

PART I.

GENERAL PHYSIOLOGY.

CHAPTER I.

THE PHYSIOLOGY OF THE CELL: CYTOLOGY.

A. LIVING SUBSTANCE: PROTOPLASM.

1. THE PHYSICAL PROPERTIES OF PROTOPLASM.
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3. THE MORPHOLOGY OF LIVING SUBSTANCE.
    - *a*. The Structure of Protoplasm.
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        - (1) *Cytoplasm.*
        - (2) *The Nucleus: Nucleoplasm.*
        - (3) *The Centrosome.*
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B. THE PHENOMENA OF LIFE.

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        - (1) *Chemical Phases.*
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2. MOTOSENSORY ACTIVITIES OF LIFE.
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A. LIVING SUBSTANCE: PROTOPLASM.

1. THE PHYSICAL PROPERTIES OF PROTOPLASM.

One's knowledge of a substance is gained through the senses. The most far-reaching sense—vision—is the one usually appealed to first, and one naturally determines first of all whether the substance is solid or fluid, whether it is transparent or opaque. Through other senses one determines whether the substance is heavy or light, etc.

Protoplasm exists only in minute portions, so mixed with the substances which it has formed that it is visible only through the aid of a microscope. That instrument reveals protoplasm as *a viscous fluid.* The consistency is more fluid in the active protoplasm of a growing plant or animal than in the dormant protoplasm of a seed. Whether protoplasm is thin viscous or thick viscous in consistency depends upon the amount of water which it imbibes. Seeds sometimes become very dry. When placed in the ground they cannot germinate—the protoplasm cannot pass from its dormant condition into an active one—until they first absorb water, a portion of which is absorbed by the protoplasm and a portion by the stored nutriment of the seed.

In thin layers or threads *protoplasm is gray and translucent.* In thick threads or globules immersed in water it is shown to be *somewhat more strongly refractive than the water.*

When a minute organism or cell, consisting of a drop of protoplasm enclosed in a delicate membrane, is studied in distilled water, it will be observed to swell up, almost bursting the enclosing membrane, but there is no evidence that any of the protoplasm passed through the membrane. If one immerses the organism in a 5 per cent. salt solution it will shrivel, indicating that something has passed out of the membrane, but there is no evidence that any of the protoplasm has passed through the membrane. *Protoplasm imbibes water, but it is not diffusible.*

Incidental to the observations just described it would be noticed that the protoplasmic organism sinks to the bottom of the distilled water, and rises to the top of the strong salt solution—it is heavier than distilled water, and it is lighter than the salt solution. *Protoplasm has a specific gravity greater than* 1. If one were to increase the specific gravity of the surrounding liquid until the protoplasmic body would just float, neither rising nor falling, he would have only to determine the specific gravity of the liquid to know that of the protoplasm. In this way Jensen, in 1893, found the specific gravity of a paramecium to be 1.25. Living organisms may change their specific gravity through the absorption and deposit of heavy mineral substances, such as $CaCO_3$ or SiO_2, or through the formation and retention of such substances as carbonic acid gas or fat.

2. THE CHEMICAL PROPERTIES OF PROTOPLASM.

As nature's unaided vision reveals nothing of the physical properties of protoplasm, so does her unaided taste and smell reveal nothing of the chemical properties of protoplasm. We bring to the aid of these primitive chemical tests refined process of analysis, through the aid of which one gains a knowledge of the elements which combine to form protoplasm. Pure protoplasm has not been analyzed, because it cannot be obtained in sufficient quantity.

There are reasons for believing that pure protoplasm does not differ much from albumen in composition. Egg albumen must contain all of the elements found in protoplasm, because the protoplasm of the chick is built up from the albumen of the egg. Albumen consists of carbon, hydrogen, nitrogen, oxygen, and sulphur, with certain mineral salts, associated in loose chemical combination—salts which represent phosphorus, chlorine, sodium, potassium, calcium, iron, and magnesium. The analysis of the bodies of animal and plant organisms reveals the universal presence in these bodies of the following elements: C, H, N, O, S, P, Cl, Na, K, Ca, Mg, and Fe. Rarely one or more of the following elements is found: Si, Li, Fl, I, Br, Al, Mn, and As.

Just why living matter should be constructed from the elements named, rather than from such elements as lithium, berylium, boron, titanium, chromium, zinc, lead, etc., has been the subject of some controversy. Verworn (*Allgemeine Physiologie*, p. 106) calls attention to the fact that the elements of which living matter is composed are elements of light atomic weight. The following table may throw some light upon the question:

TABLE SHOWING THE RELATION OF ATOMIC WEIGHT AND DISTRIBUTION TO SELECTION BY LIVING ORGANISMS.

ELEMENTS in order of importance to life.	O, H, C, N, S, P, Cl, Na, K, Ca, Fe, Mg,——Si, Li, Fl, I, Br, Al, Mn.
In order of atomic weight. Line *a*, found in life; *b*, sometimes found; *c*, never found in life.	*a*. H=1, C=12, N=14, O=16, Na=23, Mg=24, P=31, S=32, Cl=35.5, K=39, Ca=40, Fe=56. *b*. Li 7 . . . . Fl=19 . . Al=27, Si=28 . . . . Mn=55 . . . . As=75 . . . . Br=80 . . . . I=127. *c*. Be=9.4, Bo=11, Ti=48, Ni=58.5, Zn=65, Se=79, Zr=90, Ru, Ag, Sn, V=51, Co=59, Ga=69, Rb=85, Ni=94, Ro, Cd, Cr=52.5, Au=68, . . . Sr=87.5, Mo=96, Pd, In, and about 25 more elements.
In order of distribution on the earth's surface.	O, H, C, N, Ca, Fe, Cl, Na, K, Li, Mg, Si, S, P, Al, I, Br, Fl, Mn, etc.

O = $^1/_5$ atmosphere, $^8/_9$ H_2O, 44–48 per cent. of solid crust.
H = $^1/_9$ H_2O in air and among rocks.
C = (CO_2) in air and in solution in H_2O.
N = $^4/_5$ air, in solution in H_2O, in nitrates of soil.

The facts above tabulated justify one in making two generalizations: (1) The elements which enter into the composition of living substance are, in general, those of lightest atomic weight. (2) The elements which enter into the composition of living substance are, without exception, abundant elements of wide—practically universal—distribution.

The chemical compounds which are found in living matter may be divided into organic and inorganic. The organic compounds may be classified as proteins, fats, and carbohydrates. The proteins are very similar to living protoplasm in composition. As an example of proteins, one may take pure egg albumen, whose formula, according to Hofmeister, is $C_{204}H_{322}N_{52}O_{66}S_2$. All proteins contain C, H, N, O, and either S or P. The nucleoproteids contain phosphorus. Fats and carbohydrates are non-nitrogenous substances. The typical fat—tripalmitin—has the formula $C_3H_5(C_{16}H_{32}O_2)_3$. The typical carbohydrate—glucose—has the formula $C_6H_{12}O_6$. Note that these compounds are both formed of carbon, hydrogen, and oxygen, and that the proportion of oxygen in the fat is very much smaller than that in the carbohydrate. Some of the inorganic compounds associated with living matter are: $NaCl$, Na_2CO_3, Na_2HPO_4, $Ca_3(PO_4)_2$, $NaHCO_3$, $MgCl_2$, $KHSO_4$.

3. THE MORPHOLOGY OF LIVING SUBSTANCE.

a. The Structure of Protoplasm.

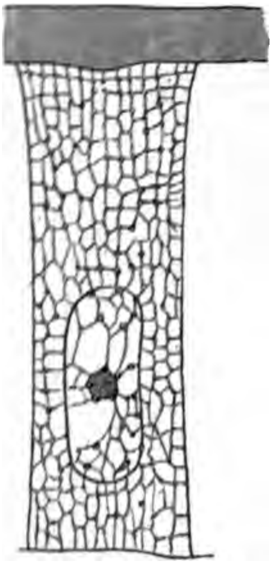
If protoplasm be studied under very high powers of the microscope it will present an appearance such as shown by Bütschli in the accompanying figures (Figs. 1 and 2). This appearance has been differently interpreted by different observers. Bütschli and his followers contend that protoplasm is a "foam-like, alveolar structure, like an emulsion, in which the firmer portion forms the walls of separate chambers filled with the more liquid substance." (Wilson.) Fleming, Van Beneden, Strasburger, and others believe "that the more solid portion consists of coherent threads which extend through the ground substance," usually forming a fine meshwork or *reticulum*. (Wilson.) Adopting the more generally accepted second interpretation, we have protoplasm represented by two substances: (1) the more dense and refractive reticulum, or *spongioplasm*, and (2) the less dense, ground substance, *cytolymph*, or *hyaloplasm*. Lower powers of the microscope reveal minute granules which are shown by Bütschli's figures to be located in the threads of the reticulum or spongioplasm. Some of the granules may be only apparent, and represent the confluence of several threads of spongioplasm; but some are undoubtedly actual granules of living substance.

These granules are called *microsomes*, and have been held by some investigators to be the "elementary units of structure standing between the cell and the ultimate molecules of living matter." (Wilson.)

b. The Structure of the Cell.

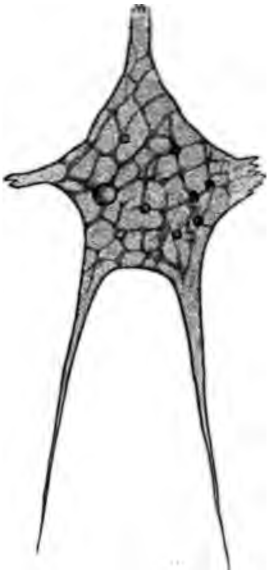
Living substance or protoplasm exists only within structures called cells. The early microscopists saw the little polyhedral, cellulose chambers of plants, and chose the word cell as most appropriate. The contents of this little chamber were collectively called protoplasm by Mohl (1846), but its importance was overlooked. Schultze, Kölliker, and others recognized finally that the protoplasm is essential, and that the cell wall is unessential; the amœba and the white blood corpuscles, for example, having no cell wall. Schultze (1863) defined the cell as "a simple globule of protoplasm containing a nucleus." After the discovery of the centrosome by Van Beneden (1876) it became necessary to define the cell anew. In 1890 Bauer defined it as "a globule of protoplasm containing a nucleus and centrosome." But certain lower forms of life, as most bacteria, have no nucleus or centrosome. In 1895, Verworn, of Jena, defined the cell as "a body consisting essentially of protoplasm in its general form, including the unmodified cytoplasm, and the

FIG. 1



Epidermal cell of an earthworm (× 3000).

FIG. 2



Expanded end of a rhizopod's pseudopod (× 3000).

specialized nucleus and centrosome; while as unessential accompaniments may be enumerated: (1) the cell membrane, (2) starch grains, (3) pigment granules, (4) oil globules, and (5) chlorophyll granules." Wilson (1896) most clearly defines the typical cell diagrammatically (Fig. 3). A careful study of this diagram in connection with Graf's drawing of a nephridial cell from a leech (Fig. 4) will give the reader a clear conception of the present knowledge of the structure of the cell. The living substance of the cell is called protoplasm. That portion of the living substance which is outside of the nucleus is called *cytoplasm*, while the living matter of the nucleus is called *nucleoplasm*.

FIG. 3.

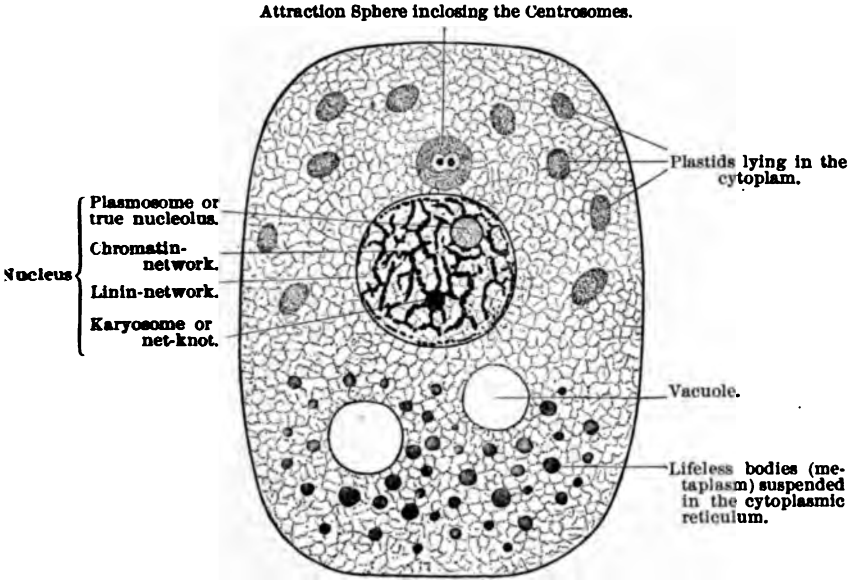
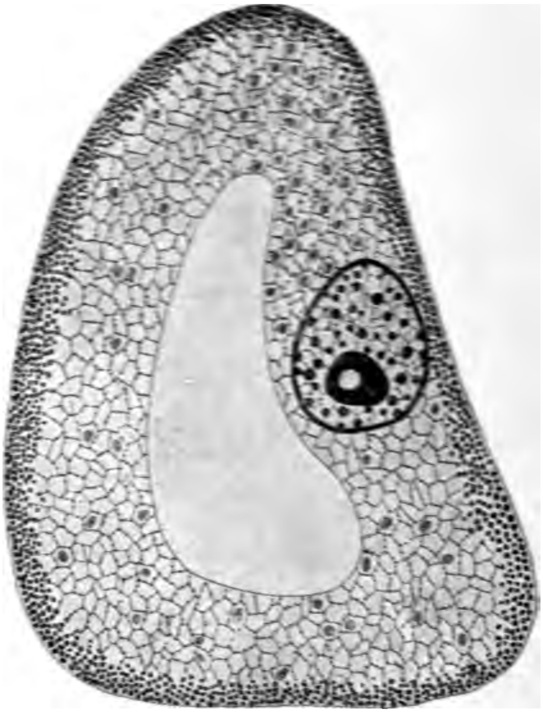

Attraction Sphere inclosing the Centrosomes.
Plastids lying in the cytoplasm.
Nucleus
Plasmosome or true nucleolus.
Chromatin-network.
Linin-network.
Karyosome or net-knot.
Vacuole.
Lifeless bodies (metaplasm) suspended in the cytoplasmic reticulum.

Diagram of a cell. (After Wilson.)

1. **Cytoplasm.**—In most unicellular organisms, and sometimes in animals of higher rank, the cytoplasm is differentiated into the inner endoplasm and a somewhat denser exoplasm. The latter produces the cell membrane when that is present, or in its absence takes its place. Cilia are outgrowths from the exoplasm. Wilson calls attention to the fact that "it appears to be a general rule that the nucleus is surrounded by protoplasm of relatively slight differentiation (endoplasm), while the more highly differentiated products of cell activity are laid down in the more peripheral region of the cell." The fact that the reticulum of the cytoplasm has not been found in all cells—especially certain plant cells—leads some biologists to look

upon it as an incidental or even accidental structure rather than a typical one. Besides the division of the protoplasm into exoplasm and endoplasm it may be divided into spongioplasm and cytolymph. The *spongioplasm* may be represented by the reticulum made up of threads of dense protoplasm in which the *microsomes* float, or, in the absence of a reticulum, the spongioplasm is represented only by the microsomes which float in the cytolymph. The ***plastids*** are differentiations of the cytoplasm. They are capable of growth and division. They may be looked upon as metabolic organs of the cell. They form starch grains, chlorophyll grains, or pigment corpuscles, from constituents of the cytolymph. Those that form starch grains

Fig. 4



Section through a nephridial cell of the leech, *Clepsine*. Drawn by Arnold Graf from one of his own preparations.)

The centre of the cell is occupied by a large vacuole, filled with a watery liquid. The cytoplasm forms a very regular and distinct reticulum with scattered microsomes, which become very large in the peripheral zone. The larger pale bodies, lying in the ground-substance, are *excretory granules* (*i. e.*, metaplasm). The nucleus, at the right, is surrounded by a thick chromatic membrane, is traversed by a very distinct linin network, contains numerous scattered chromatin granules, and a single large nucleolus within which is a vacuole. (Wilson, The Cell in Development and Inheritance, 1896.)

are called *amyloplasts*, those that form chlorophyll are called *chloroplasts*, and those that form pigment grains are called *chromoplasts*. Enclosed within the cytoplasm, and formed from it either by the plastids, the nucleus, or otherwise, are many lifeless products of cell metabolism—starch grains, chlorophyll grains, pigment grains, oil globules, excretory granules, etc. Some of these represent reserve nutriment and some of them waste matter. The *vacuole* is a globule of food material or of waste material in solution. It is seen only in lower forms of plant and animal life.

2. **The Nucleus: Nucleoplasm.**—"A fragment of a cell deprived of its nucleus may live for a considerable time, and manifest the power of co-ordinated movement without perceptible impairment. Such a mass of protoplasm is, however, devoid of the powers of assimilation, growth, and repair, and sooner or later dies. In other words, those functions that involve destructive metabolism may continue for a time in the absence of the nucleus; those that involve constructive metabolism cease with its removal. The nucleus is generally regarded a controlling centre of cell activity, and hence a primary factor in growth, development, and the transmission of specific qualities from cell to cell, and so from one generation to another." (Wilson.)

(*a*) **The Structure of the Nucleus** is shown, in a general way, in the diagram of the typical cell (Fig. 3). Note, in that figure, (*α*) the nuclear membrane; (*β*) the nuclear reticulum divided into (1) the *chromatin reticulum*, and (2) the *linin reticulum;* (*γ*) the nucleoli represented by (I) the true nucleolus or *plasmosome*, and (II) the net-knots or *karyosomes;* (*δ*) the nuclear sap or *karyolymph* which fills the meshes of the network.

(*b*) **The Chemistry of the Nucleoplasm** may be briefly summarized: (*α*) *Chromatin* is the substance which forms the chromatin reticulum and the karyosomes. (*β*) *Linin* is the substance which forms the linin or achromatic network. (*γ*) *Paralinin* forms the karyolymph or nuclear sap. (*δ*) *Pyrenin* forms the plasmosomes. (*ε*) *Amphipyrenin* forms the substance of the nuclear membrane. It is probably identical with linin. (Wilson.)

3. **The Centrosome.**—This body is now generally regarded as the especial organ of cell division and in this sense as the dynamic centre of the cell. The centrosome was discovered and described by Van Beneden (1876–1883), and named by Boveri (1888). The structure of the resting centrosome is sufficiently shown in the diagram of the cell. It is shown there lying in the cytoplasm beside the nucleus—its typical position—though it may lie within the nuclear membrane. The function of the centrosome is so prominent a part of the process of cell division that it will be described under reproduction of the cell.

3. The Form and Size of the Cell.

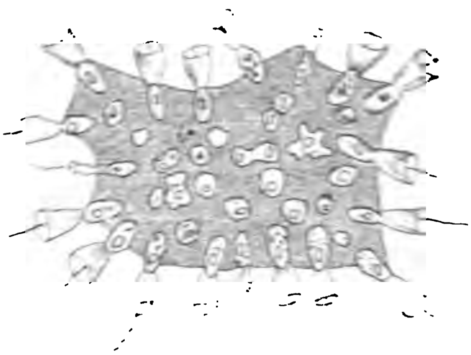
The simplest form is spherical, but many factors work together to modify this primitive form, so that one may find cells that are regularly or irregularly spherical, polyhedral, prismatic, cylindric, discoidal, fusiform, or linear. Some cells, as the ganglion cells, may be too irregular to admit of any of these rather definite terms.

The ovarian egg of the bird or reptile is a cell, which differs from the typical cell only in having a prodigious store of fat and other food materials, thus stored for the nourishment of the developing animal. The ovarian egg of an ostrich is several centimetres in diameter. On the other hand, some cells are exceedingly minute. Eberth's typhoid bacillus is about 0.9 μ in diameter—*i.e.*, eleven thousand, lying side by side, would hardly reach one centimetre. The average animal cell is about 10 μ in diameter.

4. THE INDIVIDUALIZATION OF LIVING SUBSTANCE.

Definition.—*An organic individual is a unified mass of living substance in a form capable of maintaining itself.* The smallest mass of living substance capable of maintaining itself is a cell. The cell is, therefore, an elementary organism; it is, at the same time the lowest order of individual, or an individual of the first order. *Ex.:* Amœba, Paramecium, Stentor, Vorticella, Desmid, Yeast-cell, Protococcus, Ovum, Leukocyte. Note that, in the examples cited, all but the last two are actual, independent indi-

FIG. 3.

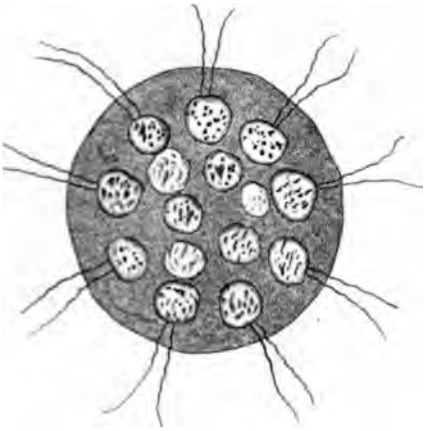


Protospongia Haeckelii, an individual of the II. order.

viduals leading a separate existence; while the ovum is a single cell capable of producing an individual capable of self-maintenance, and the leukocyte is virtually and potentially an individual, but it has merged its individuality in that of the great organism of which it is a part. Thus we may find two series of examples, one representing actual and one virtual individuals. The latter, in turn, may be subdivided into a series representing individual development (ontogenic series) and one representing stages of tissue development.

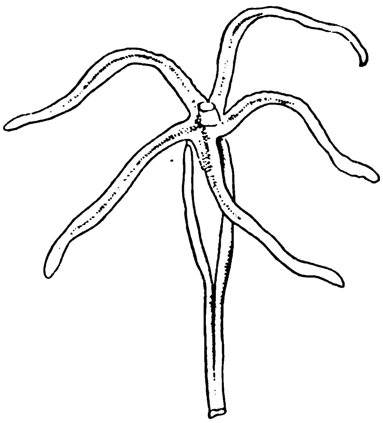
Colonies of cells, similar as to form and function, constitute individuals of the **second order.** Ex.: Protospongia, Eudorina, Morula or Blastula stage of development, cartilage. In the animal kingdom Protospongia Haeckelii (Fig. 5), and in the plant kingdom, Eudorina elegans (Fig. 6), furnish us examples of *colonization and combination for mutual help and protection.* This marks a long step in the advance of living organisms, but all of the cells are practically alike in form and function.

FIG. 6



Eudorina elegans, an individual of the II. order.

FIG. 7



Hydra, an individual of the III. order.

A unified mass of living substance, composed of two or more colonies of similar cells—two or more tissues—forms an individual of the **third order.** Ex.: Hydra (Fig. 7), the Thallophytes among plants, Gastrula stage of embryonic development, any organ, as the stomach. This marks another long step in organic evolution—*specialization of structure and function.*

Individuals of the **fourth order** are composed of organs, tissues, and cells arranged in systems, such as the digestive system. Ex.: Man, Tree. Men and other animals organize Colonies or States which represent individuals of the **fifth order**. The following table gives a general view of the individualization of living substance:

	Order.	Actual Individuals, Taxonomic Series.		Virtual Individuals.	
		Animals.	Plants.	Ontogenic Series.	Histologic Series.
Individualization of Living Substance.	I.	Amœba. Paramecium. Vorticella.	Desmid. Diatom. Protococcus. Saccharomyces.	Ovum.	Cell: Leukocyte.
	II.	Protospongia.	Eudorina. Oscillaria. Spirogyra.	Morula. Blastula.	Tissue: Cartilage.
	III.	Hydra. Jelly-fish.	Mushroom. Sea-weeds.	Gastrula.	Organ: Stomach.
	IV.	Worm. Dog. Man.	Moss. Fern. Tree.	Fœtus. Child. Man.	Systems of organs complete.
	V.	Colony. State.	Colony. Forest.	Colony. State.	

B. THE PHENOMENA OF LIFE.

1. NUTRITION.

The general term *nutrition* includes all those activities of the organism directed toward the procuring of *food, digestion, absorption,* the chemical changes within the tissues (*metabolism*), *respiration,* and *excretion.*

a. Absorption and Excretion.

1. **Absorption and Excretion of Gaseous Material.**—Every living organism ceases to live when deprived of oxygen. Oxygen exists in a gaseous form as a constituent of the atmosphere (21 per cent.); and it is dissolved in water, so that it is accessible to terrestrial and aquatic plants and animals. For multicellular organisms the law may be stated thus: Every active cell of every living organism requires oxygen for the maintenance of activity. In the whole organic kingdom the absorption of oxygen—respiration—is associated with the excretion of carbon dioxide and water, and with the production of heat. How are we to interpret these general facts? It was formerly believed that oxygen directly oxidized the living matter in the same way that it directly oxidizes the carbon and hydrogen of a candle, this process resulting, in both cases, in the formation of carbon dioxide and water and the production of heat. Pflüger, of Bonn, found by experiment that frogs can live several hours in an atmosphere of nitrogen, and continue to produce

arbon dioxide. From this and other experiments Pflüger concluded hat "The first impulses to the chemical processes of respiration are ot given by the oxygen which enters from without; but that primarily decomposition of molecules takes place within the protoplasm, esulting in the liberation of carbon dioxide, and that hence the ncoming oxygen effects a simple restitution of the integrity of the ew molecules which are formed." *This gradual breaking up of he highly complex protoplasm into simpler bodies which combine ith oxygen, liberating the energies for the life processes, is called atabolism or destructive metabolism.*

The reverse process—*anabolism* or *constructive metabolism*—is one f the most interesting and important processes in the realm of ature. Every green plant absorbs, as food, *carbon dioxide* and *ater;* these are taken into the protoplasm, and, under the influence f the green plant coloring matter—*chlorophyll*—and of the *sunight* the carbon dioxide and water are combined to form dextrose $C_6H_{12}O_6$). After dextrose is once formed, the protoplasm of the ells is able to use it in the building of protoplasm.

In recapitulation we may say, then: (1) *All living cells absorb ree oxygen in their respiratory process.* (2) *All living cells excrete arbon dioxide in their respiratory process.* (3) *All green plant cells bsorb carbon dioxide as food.* (4) *All green plant cells excrete oxygen s a waste product in their nutritive process.*

2. **The Absorption and Excretion of Liquid Substances.**—Most f the water used in the plant economy is absorbed in the fluid tate. Much water leaves the bodies of both plants and animals n the form of gas or vapor, but a large part of this is not the product f excretion, it is the product of evaporation. All of the water used in he animal economy is absorbed in the fluid state. Moreover, all norganic matter is absorbed into cells in the form of solution in water. With few exceptions it is also true that the food of most nimals, though received into the alimentary canal in the solid tate, is changed to the fluid state—by solution in water—before t is absorbed by the cells which line the alimentary canal. A most nteresting problem presents itself at this point—*the selective powers f living cells.* Living side by side in the sea are one-celled animals —some species bearing silicious shells, while other species bear alcareous shells. The first species has selected the silica from he sea-water, while the second has selected the calcium carbonate. Growing side by side in the shallow sea-water may be several species f the seaweed—Fucus—but each species will have selected different but constant proportions of the mineral matter dissolved in the ea-water. The following table from Pfeffer, cited by O. Hertwig, illustrates the point in question:

Ash-constituents		Fucus Vesiculosus	Fucus Nodosus	Fucus Serratus	Laminaria Digitata
Potassium oxide	K_2O	15.23	10.07	4.51	22.40
Sodium oxide	Na_2O	24.54	15.39	11.17	24.09
Calcium oxide	CaO	9.78	12.30	16.35	11.86
Silica	SiO_2	1.35	1.30	1.46	1.56

In the bodies of higher animals each cell is bathed in blood, or lymph, containing many food materials in solution; but the bone cells select the $CaCO_3$ and $Ca_3(PO_4)_2$, while the muscle cells select, from the nutrient fluid, proteins with various salts; and so on, every cell selecting the needed food, and rejecting what is not needed.

3. **The Absorption of Solid Bodies.**—Can living cells absorb and appropriate as food solid bodies? This can only be accomplished by cells devoid of a cell membrane, or cells having holes in the membrane. As most cells are enclosed in a membrane it is clear that the absorption of solid bodies is limited to naked animal cells—*i. e.*, to the Rhizopoda and Ciliata among lower animals, and to leukocytes, and possibly ciliated epithelium, among higher animals. Among the higher animals the power to absorb solid particles seems to be possessed by leukocytes alone; and this power is of great importance, both in health and in disease.

b. Metabolism.

The term *metabolism* is used to designate the chemical changes to which matter is subjected under the influence of life. When the chemical change combines simpler into more complex substances, the term *anabolism*, or *constructive metabolism*, is used; while for the reverse process *katabolism*, or *destructive metabolism*, is used.

1. **Chemical Phases.**—It has already been stated that under the influence of chlorophyll and sunlight the plant cell is able to cause a combination of carbon dioxide and water to form dextrose, and that the cell protoplasm has the power to use the dextrose and certain nitrogenous substances in the building up of protoplasm. Furthermore, through successive combinations with oxygen the protoplasm is, step by step, reduced to simpler compounds, until it is finally expelled from the organism in the form of carbon dioxide and water. This is, in fact, about all that is known with absolute certainty. It was formerly believed that the combination of carbon dioxide and water was direct, and as follows: $6CO_2+6H_2O=C_6H_{12}O_6+6O_2$; but it is now believed that the combination is indirect, and somewhat as follows: $CO_2+H_2O=O_2+CH_2O$ (Formic Aldehyde) and $6CH_2O=C_6H_{12}O_6$ (Dextrose).

It has been convenient to describe the two extreme steps of the process of metabolism, first the combination of the inorganic elements of our environment—CO_2 and H_2O—within a green plant cell, under the influence of the energy of the sunlight, to form dextrose, and finally the katabolism, or destructive metabolism, of the animal cell into the same inorganic elements. Between these two extremes are many intermediate steps.

In *the plant kingdom* the steps are ascending ones. The protoplasm of the plant cell is able to make a long list of carbohydrates, then of fats and oils, then of proteins, and, finally, to replenish its own substance, or to make protoplasm. The slight activities of the plant require katabolism of living substance for the liberation of the needed energy, but, on the whole, anabolism, or constructive metabolism, predominates, and the plant kingdom bequeaths to the animal kingdom a rich legacy of starch, cellulose, sugar, oils, and proteins.

Animals, on the other hand, are unable to appropriate either the free inorganic elements or the free sun energy of their environment; they depend directly or indirectly upon plants or plant products. The active life of animals involves the dissipation of much energy. This energy is liberated by the katabolism of body substance. Thus, in the animal kingdom, katabolism, or destructive metabolism, predominates.

FIG. 8

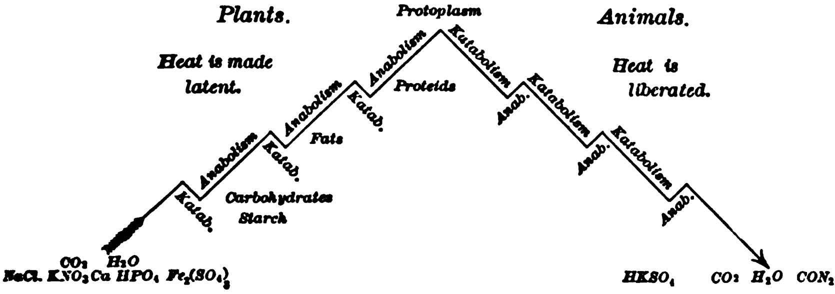


Diagram illustrating the relation of plants and animals to anabolism and katabolism.

Fig. 8 illustrates the relation of anabolism and katabolism—of constructive and destructive metabolism in the plant and animal kingdoms.

In the successive metabolic changes *ferments* play a very important part. A ferment is a protein body capable of causing a chemical change without itself being consumed or essentially altered. It is clear from this definition that a very small amount of ferment is able to accomplish a very large amount of work. Examples: Saccharomyces, Diastase, Ptyalin, Pepsin, etc.

2. **Physical Phases.**—Incidental reference has already been made to the liberation of energy and to the making latent of energy. As stated in the introduction, the law of the conservation of energy applies to animal bodies as it does to a steam engine.

(a) **The Cell's Source of Energy.** (α) CHEMICAL ENERGY.—*The combination of atoms into molecules leads to a liberation of energy while the separation of a molecule into its atomic elements requires energy.* For example, the combination of hydrogen and oxygen into water liberates heat, while the decomposition of water into its constituents requires the expenditure of energy. But in the usual chemical reaction there is both a separation and a combination of the atoms.

This leads to the formulation of the following law: *If in a chemical reaction stronger affinities are satisfied than broken, energy will be liberated; if, on the other hand, stronger affinities are broken than satisfied, energy will be required to bring about the reaction.*

Examples:

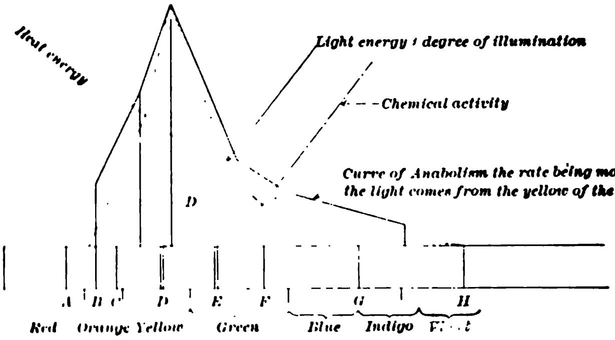
(I) Xylose, $C_6H_{10}O_6+6O_2=CO_2+5H_2O+\text{Energy}$.

Expressed verbally: Wood oxidized produces carbon dioxide and water and liberates the energy which was latent in the wood.

(II) $6CO+6H_2O+\text{Energy}=C_6H_{12}O_6+6O_2$.

Expressed verbally: Carbon dioxide and water are combined under the influence of the energy of sunlight to form dextrose, which is a complex molecule representing latent energy. Oxygen is released in the process.

FIG. 9



Pfeffer's diagram showing the relation of light to assimilation in chlorophyll-bearing plants.

Potential chemical energy is the common source from which spring all the other forms of energy involved in the phenomena of life.

(β) HEAT AND LIGHT ENERGY.—The source of this form of energy for the realm of living nature is sunlight, and, as previously stated, it makes its entrance into this realm through the chlorophyll-bearing plant cell. Moreover, not all of the energy of sunlight is thus utilized; the cell selects energy as it does matter. Pfeffer's observations may be graphically presented in the accompanying figure. (See Fig. 9.) As to the action of the warmth of the sun's rays upon animal metabolism, it is rather indirect than direct, as it simply economizes animal heat and so decreases katabolism or destructive metabolism. The same may be said of such artificial measures as shelter, clothing, and heating—they all economize animal heat, thus decreasing katabolism.

(*b*) **The Cell's Manifested Energy.**—This appears in the form of cell motion, of heat, and in certain organisms in the form of light or of electricity.

2. MOTOSENSORY ACTIVITIES OF LIFE.

Recall Spencer's definition of Life: "Life is the continuous adjustment of internal relations to external relations." The same idea may be stated in slightly different terms: *Life in an organism, is a correlation of energies, manifested by a continuous adjustment of its internal activities to its environment.*

All the activities of an individual may be divided into two classes: (I) *Egoistic Activities*—which contribute to self-preservation; Egoism; Individualism. (II) *Phyletic Activities*—which contribute to the preservation of the race; Phyleticism; Altruism. In the first case we find the organism in a struggle for life—life of self; in the second case we see the organism sacrificing self for the preservation of the species. Applied more specifically to physiology, the first class of activities are those which contribute to the *procuring* of *nutriment*, to *self-defence* against danger, and, in higher animals, to the *pursuit of pleasure;* while the second class is represented by reproduction, protection of offspring, etc., and in higher animals philanthropy.

Self-defence as well as the procuring of food usually involves *motion*—frequently also locomotion—on the part of the organism. Motion is always in response to a stimulus; but response to a stimulus involves irritability. It must be evident, then, that the activities of the motosensory organs and tissues are interdependent and that they must follow a particular sequence.

a. Motion: Contractility.

For the most part the motion of living organisms is due to their possession of the property of contractility, but there are among the plants various other methods of moving the parts of the individual, or even of moving the whole individual (locomotion), than through contractility of living substance. It would seem as if nature had tried various experiments and had finally in the higher animals specialized the property of contractility as the most efficient method of producing motion.

1. **Motion without Contractility.** (*a*) **Motion through Swelling of the Cell Wall.**—The spores of the common horse-tail rush, *Equisetum*, are provided with four little cellulose appendages (elaters) which wrap tightly around the body of the spore when moist and extend when dry. The alternation of these two conditions, accompanied by an alternation of flexion and extension, causes the spore to move slowly over the surface of the soil, to some distance from the parent plant.

(*b*) **Motion through Change of Cell Turgor.**—The closing of leaves at night and their opening in the sunlight is a phenomenon known to every school child. How do the leaflets of the clover, oxalis, or sensitive plant close together? In the axil of every leaf is a motile organ composed of thick-walled parenchyma cells between the fibrovascular bundle and the epidermis below, while the fibrovascular bundle, though flexible, is not extensible. The tissues above the fibrovascular bundle are very scantily represented. When the parenchyma cells above mentioned become turgid with water the leaf-stalk is erected; if the water is suddenly allowed to escape from the cells the leaf falls to the nocturnal or sleeping position by its own weight. When the proper stimulus comes, the protoplasm imbibes water again and the leaf is erected.

(*c*) **Motion through Change of Specific Gravity.**—Certain marine animals of low rank (Radiolaria, Siphonophora) utilize their own excretions to buoy them up. By retaining their carbon dioxide it so decreases their specific gravity that they rise to the top of the water. On the other hand, by giving off the carbon dioxide, or by deposit of calcium salts or of silica within their tissues they again sink.

(*d*) **Motion through Secretion.**—The movements of desmids and diatoms were, for a long time, a subject of study. It finally became apparent that the minute organism was leaving behind it a little trail of secreted mucus, which served the double purpose of anchoring it to its place and of pushing it along.

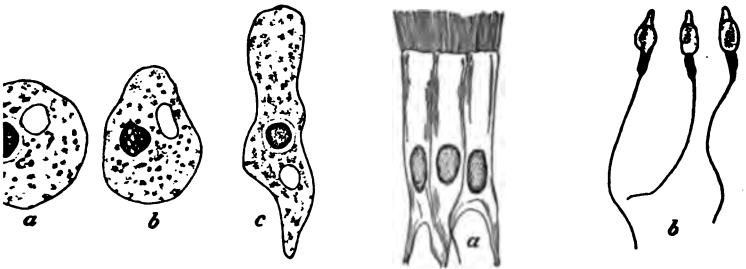
(*e*) **Motion through Growth-tension.**—The seed pod of the Touch-me-not grows in such a way that the opposite segments exert a nicely balanced tension against each other. If the ripe pod be gently pressed the equilibrium is destroyed and the pod flies to pieces, throwing the seeds out.

2. **Motion through Contractility.** (*a*) **Amœboid Motion.**—The amœba when in a state of rest is spherical, and presents to the medium in which it floats the minimum surface. Its motion consists in the pushing out of a portion of its periphery. (See Fig. 10.) This act increases the surface exposed to the medium and thus increases

ɪpportunity for the exchange of oxygen and carbon dioxide. ɪo increases the opportunity to get food. The hungry amœba ways active. The extensions of its protoplasm—its pseudo-ɪ—may be numerous, and they vary from minute to minute. form of motion is observed also in the white blood corpuscles, ukocytes.

Ciliary Motion.—Many cells are provided with fine proto-nic extensions, which are permanent and may cover the whole ce of the cell, or a limited surface, and may be numerous or In active cells the cilia are in a state of constant motion, which sts in a quick whip-like motion in one direction, followed by w return. All of the cilia on the end of a ciliated cell of the ɪn respiratory tract (Fig. 10, *B a*) move in the same direction

FIG. 10



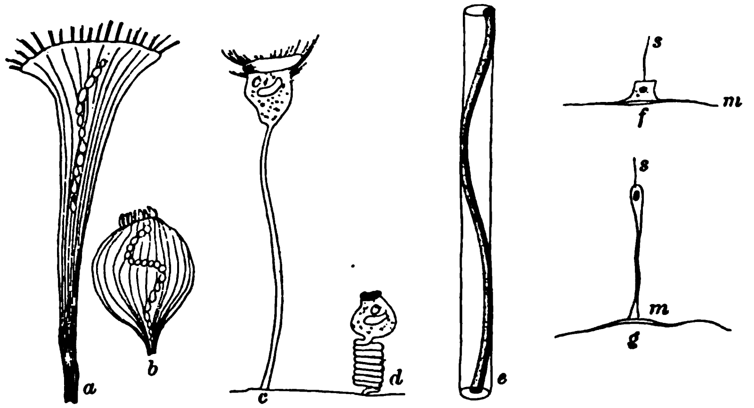
ɪœba in different phases of motion (*A b c*). Ciliated epithelial cells (*B a*). Spermatozoa with motile flagella (*B b*).

same time. Furthermore, all of the cilia of all the cells in any act in unison, producing an undulatory motion running over ole surface. The result of such a movement of the cilia is y over the surface any small particles or accumulation of ns. Cilia are capable of a prodigious amount of work. ated epithelium of a frog's œsophagus will carry a 100-mgm. ght up a 60-degree incline when the lead presents as much uare millimetres.

ɪrm of ciliary motion is that presented by the spermatozoa *B b*). Here the one cilium, or flagellum, possesses a scull-ɪn, which propels the spermatozoon through liquids or over faces.

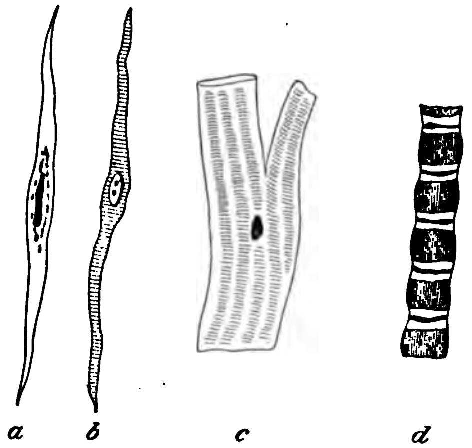
cular Motion, or Motion by Fibrillary Contractility.—A third otion is that through contraction of fibrillæ. Contractile ar very low in the animal scale. The *Stentor*, a ciliated possesses numerous fine fibrillæ in the exoplasm of the ɪgh the contraction of these fibrillæ the body may retract ttle foot until it assumes a nearly spherical form. The ed Vorticella has a long, slim pedicle to its bell-shaped body. The stalk has the property of retracting into a closely coiled spiral, a striking view under the microscope. Fig. 11, *c*, *d*, *e*, shows the mechanism which produces this remarkable effect. There is a single contractile fibril passing spirally down the inside of the sheath of the pedicle. Contraction of this fibril tends to straighten it, throwing the pedicle into a spiral. Next in the progressive series

FIG. 11



Illustrating fibrillary contractility: *a*, *stentor* open: *b*, *stentor* contracted; *c*, *vorticella* open and (*d*) contracted, with (*e*) section of pedicle of same; *f* and *g*, neuro-muscle cells of a cœlenterate. Note that the nucleated body of these cells possesses a sensitive, tactile flagellum (*s*) and a contractile fibrilla (*m*). The second one of these cells (*g*) is especially interesting because the thread of protoplasm between the body of the cell and the motor fibrilla is the functional equivalent of a motor or efferent nerve.

FIG. 12



a, non-striated muscle cell; *b*, striated muscle cell of frog's heart; *c*, striated muscle cell of mammal's heart; *d*, striated muscle cell of insect's wing.

euromuscular cell of the medusa may be named. (See Fig. *9*.)

usculat tissue is fairly well developed in Vermes, and very y developed in the higher Arthropoda, especially the Insecta. .2, *a*, *b*, *c*, shows some forms of muscle fibres or cells from verte- animals. Fig. 12, *d*, shows a portion of a fibrilla from a le fibre of an insect's wing. For a further description of the le tissue of the higher animals see the anatomical introduction e next chapter.

iscle tissue is sensitive to various stimuli applied either directly e muscle or indirectly to the nerve which supplies the muscle. i stimulated, the muscle responds by making a contraction i consists in a decrease in length with increase of the thickness, 'olume remaining the same. Other important changes take in a muscle cell incident to its contraction—viz., the chemical ges which liberate the mechanical energy of motion, and a n amount of heat energy. These changes will be discussed at h in the chapter on the Physiology of Contractile and Irritable ies.

b. Sensibility: Irritability.

e most noticeable fact observable in the Vorticella is its motion. observing this motion for a time, one asks, Why does it move? e microscope slide upon which it is resting be jarred, or if it uched by some foreign body, the contraction will take place. ntly the organism as a whole, or some specialized portion of sensitive to these mechanical stimuli.

ien the amœba, resting quietly on the slide, suddenly thrusts pseudopodium the immediate cause is not so evident. The is internal. The amœba is hungry, and, like all hungry organ- it starts upon a foraging tour. In every case motion, indeed, ll activity, is in response to stimuli. *The ability to respond to li is called irritability.* This is the characteristic of living matter gh which it is susceptible to changes in its environment; it is rimary distinguishing feature of living matter. Without it the organism, being unconscious of changes in its environment, originate no activity which would bring it into harmony with irroundings, and its destruction through hunger or accident l inevitably soon follow. A complete successful adaptative n then requires: (1) irritability; (2) motion and co-ordination ace and time.

ne stimuli are external to the organism and apparent to the ver; others are internal and not apparent. The invisible li are just as real as the visible ones. The internal stimulus starts the amœba in quest of food is probably a chemical

1. **Stimuli Classified.**—If one studies the reaction of living organisms to changes in the environment he will find that responses are induced by the action of some form of energy. The house-plant turns its leaves toward the light; the activities of the amœba are increased by a rise in temperature; the muscles contract in response to an electric shock; the Vorticella contracts its pedicle when its cilia touches a foreign object, and the activity of the yeast plant is increased by weak salt solution.

All stimuli which induce response from living organisms are represented in the classes cited above; and these classes may be enumerated (I) *Light,* (II) *Heat,* (III) *Electricity,* (IV) *Mechanical stimuli,* comprising pressure tension and vibrations (sound); (V) *Chemical stimuli.*

2. **Action of Stimuli.**—If one shade one portion of a large aquarium he will observe in a few days a marked difference in the living forms that inhabit the light and dark portions of the aquarium. The stem and leaves of plants lean toward the light, while the root naturally grows toward the dark. Chemical substances that attract some organisms repel others. One may, therefore, conclude: (I) *The same stimulus may produce quite different effects on different organisms.*

If one pinch or cut a living motor nerve the muscle which it supplies will contract. Pass an electric current through the nerve and the muscle will contract. Touch it with a hot wire and the muscle will contract. Put a few crystals of salt on the nerve and the response is muscular contraction. Look toward the window; the light stimulates the retina. Close the eye and press upon the eyeball near the exterior angle of the lids; a ring of light appears near the inner angle. From these observations one may conclude:

(II) *Different stimuli will produce the same effect in a tissue if the tissue is highly specialized.*

(III) The action of stimuli is more or less transient—*i. e.,* the stimulated organism returns after a short period, more or less completely, to its former state of rest.

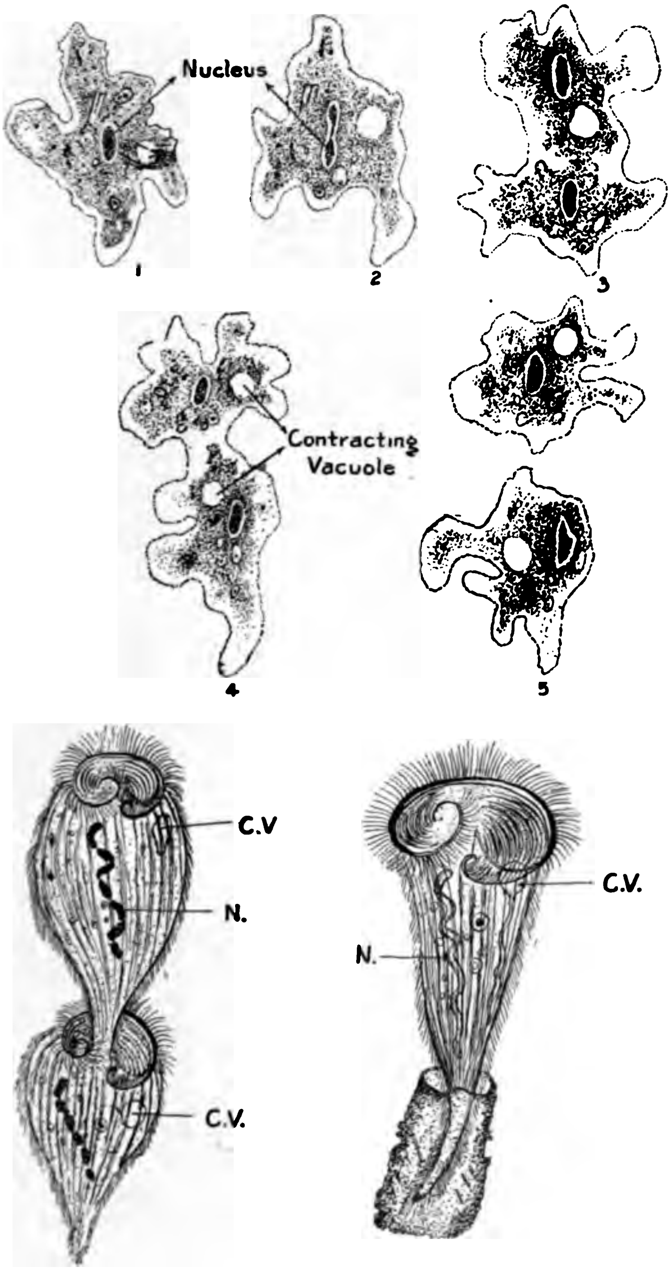
(IV) Overstimulation always leads to exhaustion, recognized at that point where even a strong stimulus fails to elicit a response.

3. REPRODUCTION.

Reproduction has already been mentioned as one of the phyletic or altruistic functions, for the reason that it invariably involves on the part of the individual sacrifice of self for species.

In a general way the lower animals undergo a greater self-sacrifice in the *reproduction* of offspring, while the higher animals undergo a greater self-sacrifice in the *support* and *protection* of offspring. Let us proceed to the description of the phenomena of cell reproduction.

FIG. 18



Direct or amitotic cell division. 1-5, division of amœba. The lower figures illustrate the division of the stentor. *N.*, nucleus; *C. V.*, contractile vacuole.

Cell Reproduction.—It was demonstrated by Virchow that every cell is from a cell—"*Omnis cellula e cellula.*"

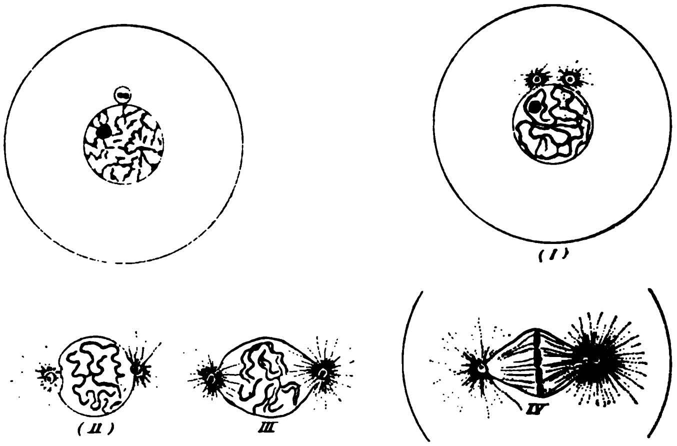
"No spontaneous generation of cells occurs either in plants or in animals. The many millions of cells of which the body of man is composed have been produced by the repeated division of *one* cell—the *ovum*—in which the life of every animal commences." (Hertwig.)

There are two methods of cell reproduction—*direct* and *indirect.*

(*a*) **In the Direct or Amitotic Method** the division of the cell protoplasm usually begins in the nucleus followed by the cytoplasm. The contractile vacuole usually takes part in the division. (See Fig. 13.) This form of cell reproduction may be observed "in glandular epithelia, in the cells of transitory embryonic envelopes, and in tumors and other pathologic formations." (Wilson.)

(*b*) **The Indirect: Mitosis or Karyokinesis.**—In this method the nucleus plays the principal role, the chromatin presenting a series of striking appearances, called the karyokinetic figures. This form of cell reproduction is now held to be typical for nearly all healthy nucleated cells.

FIG. 14

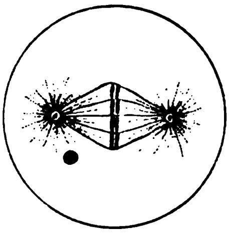


Prophases of karyokinesis: *I*, division and migration of centrosome; *II*, resolution of chromatin into well-defined thread; *III*, segmentation of same into chromosomes; *IV*, development of amphiasters; chromosomes equatorial. (Wilson.)

Karyokinesis, mitosis, or indirect cell division, presents a very long series of changes sufficiently different one from another to lead to the description of twelve to fifteen different stages. O. Hertwig and Wilson use four principal phases, one phase frequently representing several stages.

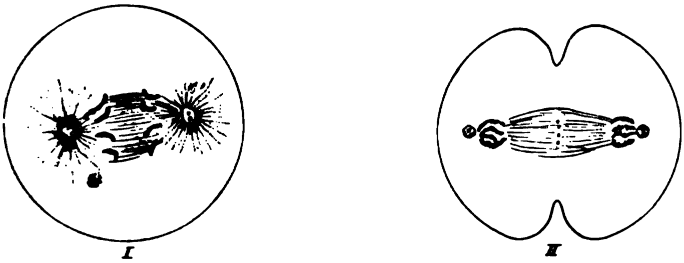
Following these authors mitosis may be thus briefly summarized: In its resting condition, which immediately precedes mitosis, one may observe a walled nucleus, with granular chromatin and a more or less clearly defined centrosome, which may have previously divided, but which is dormant.

FIG. 15



Metaphase of karyokinesis. (Wilson.)

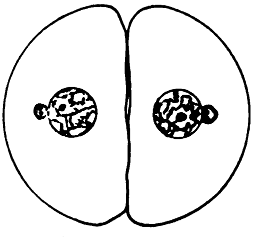
FIG. 16



Anaphases of karyokinesis. (Wilson.)

(*α*) *The Prophases* or preparatory stages. (Fig. 14.) (I) *Division* of the *centrosome* and *migration* of each young centrosome, along the circumference of the nucleus to opposite poles of the nucleus. (II) Resolution of the chromatin substance of the nucleus into a well-defined thread or spirem, which is coiled within the nucleus. (III) Segmentation of the spirem into a definite number of *chromosomes*. "Every species of plant or animal has a fixed and characteristic number (8 to 36, 16 in man) of chromosomes which regularly recurs in the division of all of its cells. In all forms arising by sexual reproduction the number of chromosomes is even." (Wilson). (IV) Development of the *Amphiaster* which consists of two polar *asters*, in the centre of each of which lies a centrosome, also the *spindle*. The aster lies in the cytoplasm, while the spindle, formed of numerous meridional fibrillæ, formed from the achromatic network, occupies the nucleus, whose walls have in the mean time disintegrated and disappeared. (V) The chromosomes assume a position in the equatorial plane of the spindle forming the *equatorial plate*.

FIG. 17



Telophase of karyokinesis. (Wilson.)

(*β*) *Metaphase*. (Fig. 15.) Longitudinal division of each chromosome. "The daughter nuclei receive precisely equivalent portions of chromatin from the mother nucleus." (Wilson.)

(*γ*) *Anaphases*. (Fig. 16.) (I) Divergence of the two sets of daughter chromosomes toward the poles of the spindle. Probably drawn by the meridional fibres of the spindle, which seem to be attached to them. (II) The divergence of the daughter asters reveals an inner spindle. This is first visible at the equator of the nucleus, and called the *interzonal fibres*. (III) Division of the centrosome preparatory to the next mitosis.

(*d*) *Telophases*. (Fig. 17.) (I) "The entire cell divides in two in a plane passing through the equator of the spindle, each of the daughter-cells receiving a group of chromosomes, half of the spindle and one of the asters with its centrosome." (Wilson.) (II) The chromatin becomes distributed in granular form, as found at the beginning. (III) The nucleus provides itself with another nuclear membrane.

CHAPTER II.

THE PHYSIOLOGY OF CONTRACTILE AND IRRITABLE TISSUES.

A. PHYSICAL INTRODUCTION.

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2. KEYS AND ELECTRODES.
3. METHODS OF MODIFYING THE CURRENT.
4. THE INDUCTORIUM.
5. THE MEASUREMENT OF ELECTRICITY.
6. GRAPHIC METHODS OF RECORDING RESULTS.

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    a. REFLEX ACTION.
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    c. NERVE CENTRES.
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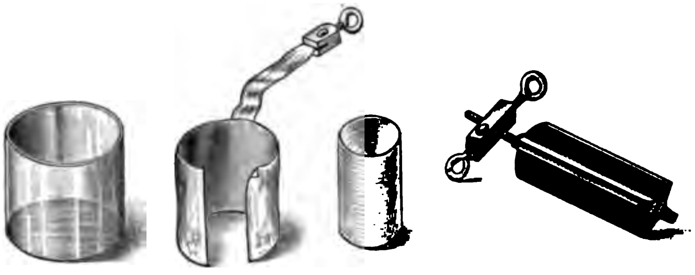
A. PHYSICAL INTRODUCTION.

Incident to the investigation of the properties of muscles and of nerves, various stimuli are employed. The stimulus most used is electricity. It is taken for granted that the student has made himself acquainted with the general principles of electricity before beginning the study of physiology. The electric appliances used in the physiologic laboratory being somewhat specialized, require a brief description.

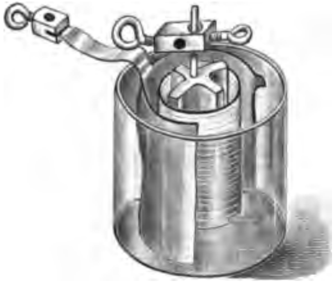
1. ELEMENTS AND BATTERIES.

The Daniell element or cell is used most in the physiologic laboratory. Fig. 18 shows such a cell to be composed of four parts:

FIG. 18



Glass jar. Copper plate. Porous porcelain cup. Zinc plate.

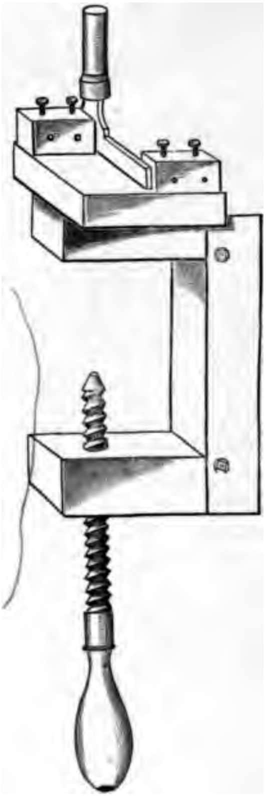


Cell assembled.

The Daniell cell.

The outer glass receptacle usually of one or two quarts' capacity; the copper plate, a thin sheet of copper; the porous cup, of unglazed vare, and the zinc plate, which stands in the porous cup. niell cell is a two-fluid cell: Outside of the porous cup, and ding the copper plate, there is a satu- lution of copper sulphate; inside of , surrounding the zinc plate, there er cent. sulphuric acid. The zinc ıst have its surface amalgamated to its too rapid consumption and the n of hydrogen gas. The zinc plate is itive plate, while the copper plate is ative one. Upon each plate there ding screw, through which the wires fixed to the plates. The distal ends wires are called the poles or elec- The electrode, which is attached negative (copper) plate, is the posi- :trode or *anode*, while the electrode, s attached to the positive plate, is gative electrode or *kathode*. No l action takes place in the cell until trodes are brought into contact with ıer, when zinc is consumed with the on of zinc sulphate and the libera- nascent hydrogen; the latter dis- rom the copper sulphate of copper, deposited upon the copper plate. amount of electric energy liberated cell is frequently insufficient to meet uirements of a physiologic experi- In such a case recourse is had to tiplication of cells to form a *battery*. ;h resistance of animal tissues to the of an electric current makes it y to adopt a particular method of joining up the cells of the —*i. e.*, the cells are joined up *in series* or *tandem*.

Fig. 19



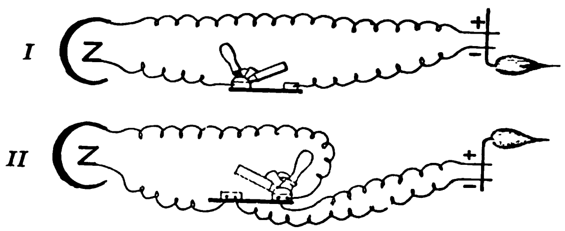
The Du Bois-Reymond key.

2. KEYS AND ELECTRODES.

key most used in physiologic experimentation is the Du Bois- ıd key. (See Fig. 19.) This key has the advantage of ng two distinct uses: (I) as a simple contact key, (II) as a cuiting key. It is evident in the second case that when the losed the current is "short-circuited," and passes from the to the negative side through the key. When the key is as shown in Fig. 20, *II*, the current is thrown into the longer circuit and must traverse the nerve which lies upon the electrodes. This is the usual method of using the Du Bois-Reymond key, especially with induced currents.

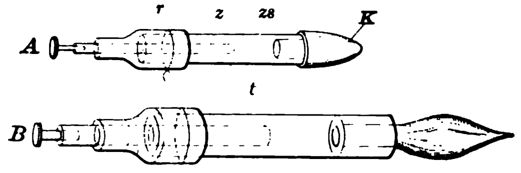
When a constant current passes from metallic electrodes into animal tissue there is a decomposition of the tissue fluids and a gradual polarization of the electrodes which disturbs the results of the experiment. To avoid this various non-polarizable electrodes have been devised. (See Fig. 21.) The non-polarizable electrode shown in Fig. 21, *A*, consists of a glass tube (*t*) into which an amalgamated zinc rod (*z*) extends, immersed in a saturated solution of zinc sulphate (*zs*). The zinc rod is held in place by a piece of rubber tubing, and has a binding screw at the outer end. The end of the glass tube opposite to the zinc rod is provided with a pencil of kaolin paste (kaolin powder with NaCl 0.6 per cent.). In Fleischl's electrode (*B*) a brush is used instead of the kaolin pencil.

FIG. 20



Showing uses of the Du Bois-Reymond key.

FIG. 21



Electrodes: *A*, kaolin electrode; *z*, zinc rod; *zs*, saturated solution of $ZnSO_4$; *t*, glass tube; *K*, plug of plastic kaolin; *B*, Fleischl's brush electrode, in which a camel's-hair brush is substituted for the kaolin plug.

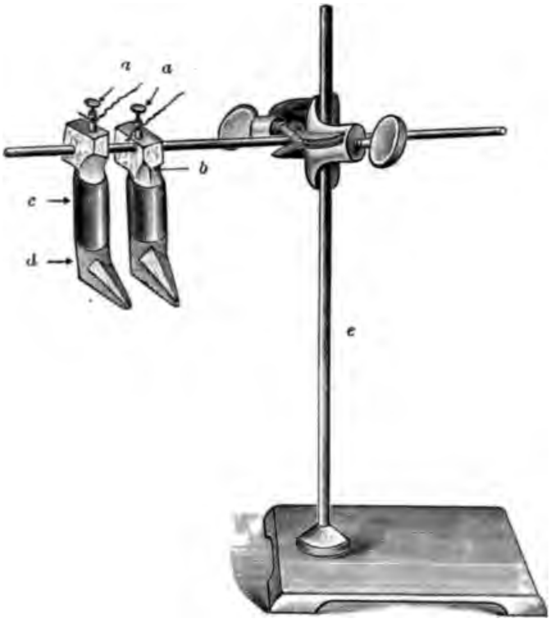
The boot electrodes utilize the principles used in the kaolin and brush electrodes, but the straight glass tubes are replaced by boot-shaped porcelain tubes with unglazed "feet." The boots stand upon the frog-board and the nerve may be laid across the "toes." This is the most convenient form of electrode for most work. (See Fig. 22.)

Work with induced currents does not require the use of non-polarizable electrodes. A shielded electrode such as shown in Fig. 23 will be found most convenient.

3. METHODS OF MODIFYING THE CURRENT.

To Change the Direction or the Course of the Current.—his a *Pohl commutator* is generally used. (See Fig. 24.) The inding posts to which the bridge is hinged may be called the

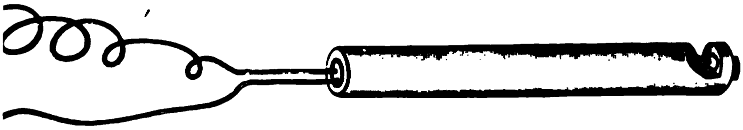
FIG. 22



The boot electrodes, non-polarizable: *a a*, binding posts; *b*, cork; *c*, glazed; *d*, unglazed; *e*, stand.

ge posts." The battery wires should be joined to these posts. cylindric handle which is used in tipping the bridge to the or the left is of non-conducting material. The current passes

FIG. 23

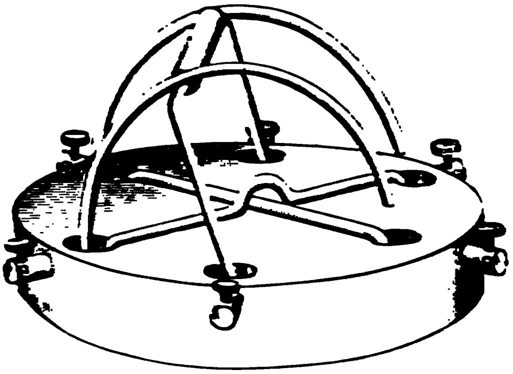


A shielded electrode of hard rubber, having copper or platinum wires.

he upright arm of the bridge, thence into the semicircular whence it passes to the mercury cup, into which the span dips, eting the circuit through the cross-bars when the bridge is tipped to the left (Fig. 25), or completing it direct when the bridge is tipped to the right. The change from one position to the other thus changes the direction of the current between the electrodes.

If the cross-bars are removed the current may be thrown at will into a circuit joined at the left-hand posts or one joined at the right-hand posts, thus changing the course of the circuit.

FIG. 24

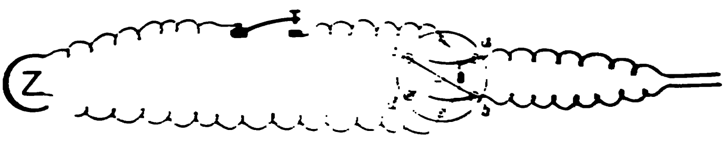


The pole changer, or the Pohl commutator.

2. **To Change the Strength of the Current.**—(*a*) The current may be increased **by the Combination of Cells in a Battery.** If the external resistance is high, which is the case in all physiologic or therapeutic uses of electricity, the cells composing the battery should be joined *in series*.

(*b*) **The Current May be Varied by Varying the External Resistance** $\left(C = \frac{E}{R}\right)$.—This may be accomplished by joining a resistance box or rheostat in the circuit. There are two ways of doing this: (I) To join the rheostat in the long circuit, by which method a removal of the plugs will decrease the current by adding resistance

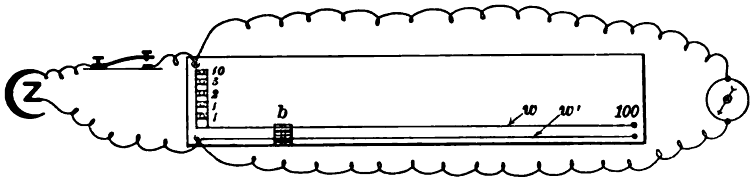
FIG. 25



Showing use of Pohl's commutator.

to its passage; (II) to join the rheostat in short circuit, by which method a removal of plugs will oppose an increased resistance to the short circuit, throwing more current into the long circuit. The first method causes a gradual decrease of the current from a maximum to a minimum; while the second and more generally employed method causes a gradual increase from zero to a maximum. The resistance box presents the disadvantage that the resistance is added or subtracted *step by step*. Many physiologic experiments require the current to change by *infinitesimal increments*. Du Bois-Reymond contrived an instrument which accomplishes this result, the rheocord (Fig. 26). The Du Bois-Reymond rheocord differs from the rheostat in substituting for the low-resistance spools two parallel platinum wires (w w'), which are connected by a bridge (b). As the bridge is slowly moved from position 0 to position 100 the resistance of the platinum wires (1Ω) is as slowly added to the short circuit. Bringing the bridge back to the zero point and removing the plug which represents 1Ω, one may slowly slide the bridge up to 100, again adding another ohm, and so on until 15 or 20Ω have been thrown into the short circuit.

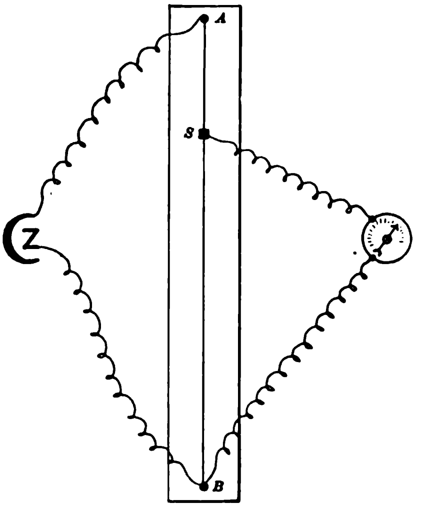
FIG. 26



Du Bois-Reymond's rheocord.

(*c*) **The Current May be Varied** by leading off or deriving any desired portion of the principal current. For this purpose one may use the simple rheocord (Fig. 27). When the principal circuit is closed the current passes from the cell to post *A* of the rheocord, along the German silver wire until it reaches the sliding contact *S*, when two ways are open to it: (i) through the wire to *B* and back to the cell, or (ii) through the galvanometer circuit. The amount of current which will pass along these two ways will be reciprocally proportional to the resistances offered by the two circuits. When the sliding contact *S* is in contact with *B* the derived or galvanometer current will be zero; when it is in contact with *A* the derived

FIG. 27



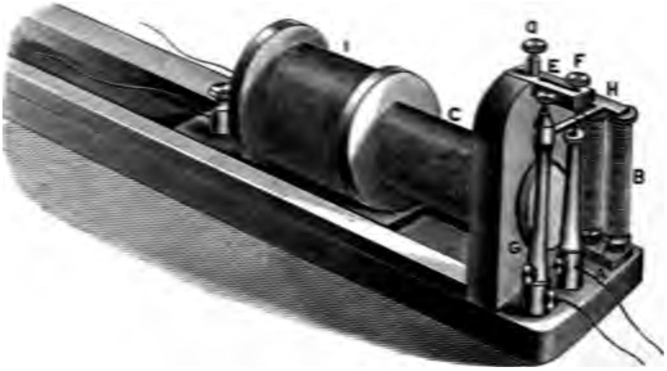
The simple rheocord.

current will be at its maximum. The principle involved in the Ludwig compensator and in the round compensator is the same as that utilized in the simple rheocord.

4. THE INDUCTORIUM.

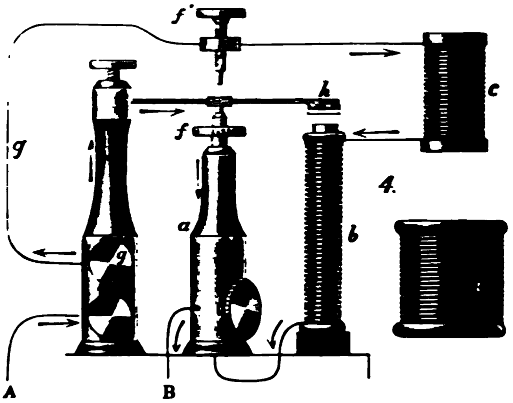
The induced current is much used in this field of experimental physiology. Several special forms of inductoriums have been contrived. That of Du Bois-Reymond is shown in Fig. 28. Two binding posts connect directly with the primary circuit. By connecting the battery to these an induced current is made every time the primary current is closed or opened. By connecting the battery wires at *G* and *A* the primary current is closed and opened automatically through

FIG. 28



The inductorium.

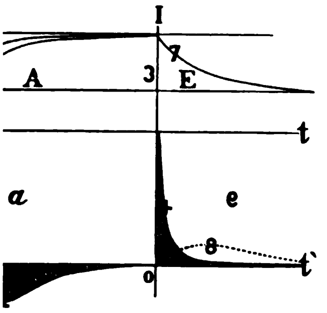
FIG. 29



Plan of Neef's interrupter.

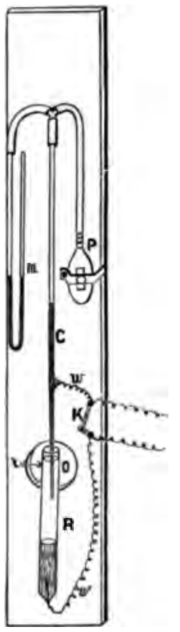
rocal action on the electromagnet *B* and the elasticity of
ner *h*. For a clearer plan of this mechanism see Fig. 29.
arrangement leads to "extra currents" in the inductorium
odify the induced current, as shown by the full lines of the
ram (Fig. 30). Von Helmholtz contrived an arrangement
the influence of the extra currents could be suspended and
ce" current equalize with the "break" current. The con-
with the screw *f′* (Fig. 29) makes the primary circuit, draws
ier down until it touches *f*, which short circuits a portion of
ry current, weakens the magnet, releases the hammer, and

FIG. 30



of the induced currents: P_1, abscissa
mary. and S_0, of the secondary current;
ing, and *E*, end of the inducing cur-
urve of the primary current weakened
ra current; 8, where the primary cur-
ened; 2 and 4, corresponding currents
n the secondary coil; P_2, height, *i. e.*,
th of the constant inducing current;
e curve of the inducing current when
ned and closed through Helmholtz's
ion; 6 and 8, the corresponding cur-
ced in the secondary circuit.

FIG. 31



Capillary electrometer.

ows all of the primary current into the long circuit. Thus
ry circuit is never broken, but rapidly varies between its
ı and minimum, as shown at 5 and 7 (Fig. 30). In the
e the induced current gives practically equal make and break
shown by the dotted lines 6 and 8.

5. THE MEASUREMENTS OF ELECTRICITY.

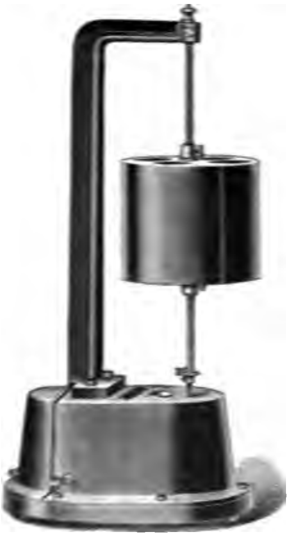
licate galvanometers of Wiedemann or of Thompson are
o the student through his work in physics. These instru-

ments are used in physiology to measure muscle and nerve currents.

Another instrument much used in physiology is the capillary electrometer, whose construction is shown in Fig. 31. The electrometer and the microscope are so mounted that all required adjustments are made by turning fine-adjustment screws. If the two platinum wires w, w' are joined up with non-polarizable electrodes, and if these are touched to portions of a body which represent different electric potential, the mercury will instantly move along the capillary, the direction of its motion indicates the direction of the muscle or nerve current, and the extent of the motion indicates the strength of the tissue electromotive force.

6. GRAPHIC METHODS OF RECORDING RESULTS.

Fig. 32



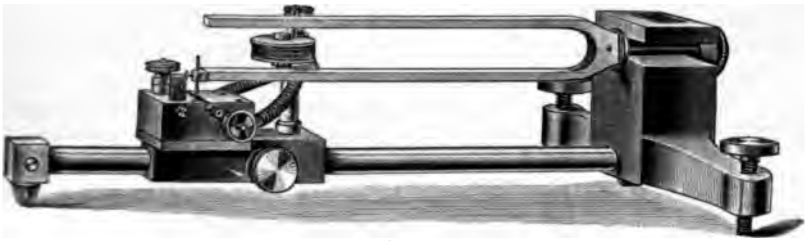
The Kymograph

This method is now universally used in laboratory experiments. The contraction of a muscle in response to a stimulus lifts a lever whose extremity is provided with a writing point. This writing point traces the movements of the lever upon a moving surface. Various devices have been employed to furnish the moving surface; the pendulum myograph, the spring myograph and the rotating cylinder. The latter appliance has come into general use for graphically recording various movements and has received the name *Kymograph* or *wave writer*. (See Fig. 32.) The instrument figured is only one of the numerous forms. Some are propelled by clock-work, some by steam or electric motor, some by weight and pulley. The form of the recorded wave depends in part upon the speed of rotation of the cylinder. The height of the wave—the ordinate—depends solely on the rise of the lever; but the outline of the wave, especially its extent along the base line—its abscissa—depends upon the relative speed of two movements: (I) the rate of rotation of the drum, and (II) the rate of movement of the lever.

The Time Record.

This is frequently necessary. In work upon the circulatory and respiratory systems it is sufficient to have a time record in seconds; such a record can be readily gotten from a contact clock which beats seconds, joined in circuit with a time-marker or *chronograph*. In muscle-nerve physiology it is necessary to record the time in shorter intervals.

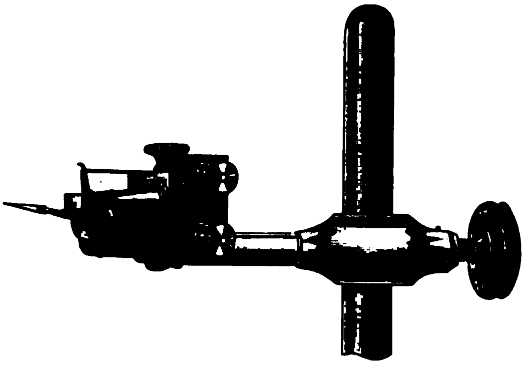
FIG. 33



The tuning fork as an interrupter.

THE TUNING FORK (Fig. 33), whose vibrations are maintained by an electric current, is usually used for this purpose. Vibrations

FIG. 34



The Deprez signal.

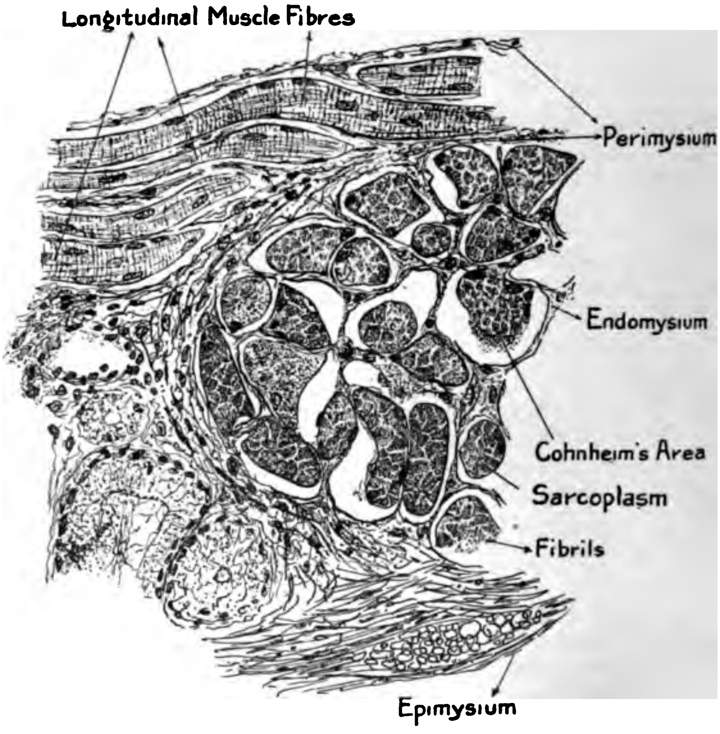
numbering 50 to 200 per second may be recorded upon a moving surface by the *Deprez signal* (Fig. 34), which is joined in circuit with the tuning fork.

B. ANATOMIC INTRODUCTION.

1. THE STRUCTURE OF MUSCLE.

The unit of structure of muscular tissue is the *muscle cell* or *muscle fibre*. The muscle cell is a multinuclear cell of prodigious size, some of them reaching a length of 12 cm. (Felix, quoted by Biederman in *Electrophysiology*), while they have a diameter ranging from 0.013 to 0.019 mm., making them easily visible to the unaided eye as fine threads. If one examine a muscle he will find it to be enclosed in a sheath of glistening connective tissue—*epimysium*—and to be readily divisible into prismatic bundles or muscular *fasciculi*, each of which is in turn surrounded by a connective-tissue sheath, the *perimysium*. The accompanying figure (Fig. 35) shows a cross-section of a fasciculus, the perimysium also being depicted. The fasciculus is in turn composed of muscle fibres or muscle cells, the spaces between which are occupied by delicate connective tissue, the *endomysium*. Note the dark spots in the periphery of the fibres. These are the nuclei.

FIG. 35

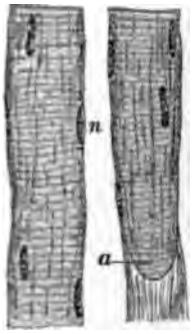


Cross-section of a fasciculus of muscle.

Each fibre or cell is surrounded by a delicate cell wall (Kölliker), the *sarcolemma*, shown in the figure as a thin black line surrounding each cell. As in the typical cell we have the cytoplasm divided into two fairly distinct substances—spongioplasm and cytolymph—so here we find structures which must represent their homologues—viz., *fibrillæ* and *sarcoplasm*. In the figure the shaded areas (areas of Cohnheim) into which the cross-section of each fibre is divided represents bundles of fibrillæ—*muscle columns*, which are separated by the sarcoplasm.

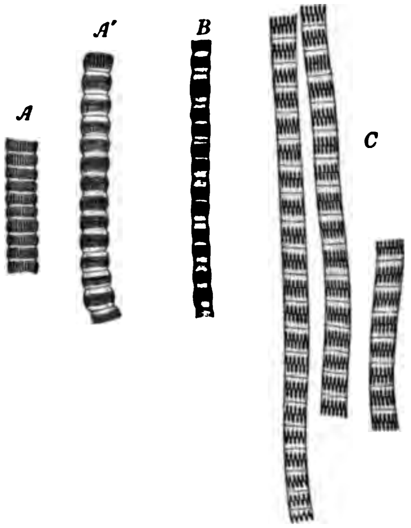
The proportion of sarcoplasm to fibrillar substance may vary enormously, both in the muscles of different animals, and in the different muscles of the same species. . . . "Those muscle fibres which serve the most persistent or most strenuous action are richest in sarcoplasm. . . . The great pectoral muscle of the best fliers (among the birds) consists exclusively, or almost exclusively, of plasmic (rich in sarcoplasm) fibres, while in the weak-winged fowls it consists predominantly of aplasmic (poor in sarcoplasm) fibres. . . . There can be no doubt that energetic chemical changes go on in the sarcoplasm, as is proved by the frequent appearance within it of fat drops. . . . All indications favor the proposition that *the sarcoplasm* furnishes the pabulum which nourishes the fibrillar substance during its activity. . . . If, then, it really is the *role* of the interfibrillar plasma (sarcoplasm) to preside over the nutrition of the contractile substance, the greater abundance of sarcoplasm in the muscles which serves the most strenuous and persistent functions is readily intelligible." (Quotations from Biederman's *Electrophysiology.*)

FIG. 36



Voluntary muscles, portions of two fibres showing the characteristic transverse markings; the lighter band is divided by the row of minute beads constituting the intermediate disk: a, termination of muscular substance and attachment of adjoining fibrous tissue; n, nuclei of muscle fibres. (Piersol.)

FIG. 37



Wing muscles of an insect.

The structure of the fibrilla has been a matter of investigation for many years. Many of the points at issue are still unsettled.

Fig. 36 shows a view of a human muscle fibre under rather high magnification. Note the alternating light and dark bands, and that the light bands are subdivided by a fine dotted line. This line is called *Krause's membrane* because it has been thought to be a membrane. The whole fibre is composed of a great number of parallel fibrillæ. Each fibrilla is segmented and presents the same alternating dark and light segments shown by the fibre as a whole. Furthermore, each fibrilla possesses a portion of the "Krause membrane." It must be evident that the areas of Cohnheim represent cross-sections of the fibrillæ.

FIG. 38

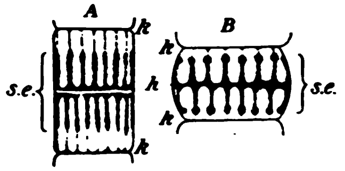
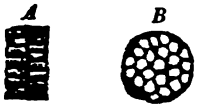


Diagram of a sarcomere: *A*, extended; *B*, contracted.

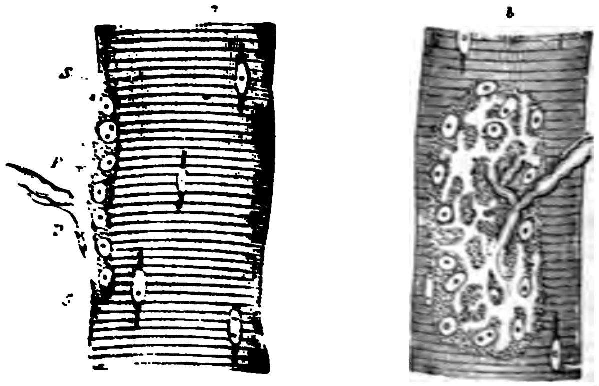
FIG. 39



Isolated sarcous elements: *A*, side view; *B*, end view.

The most favorable material for the study of the finer structure of the fibrillæ is presented by the wing muscles of insects. Schaefer's preparations shown in Figs. 38 and 39 give a very good idea of this structure. The portion between two Krause membranes is called a sarcomere. Note that in the extended condition (Fig. 38, *A*) the dark band has a light line dividing it transversely; this light line is called the line or plane of Hensen. (See Fig. 38, *A h*.) This plane of Hensen disappears when the fibrilla is contracted. (See Fig. 38, *B h*.)

FIG. 40

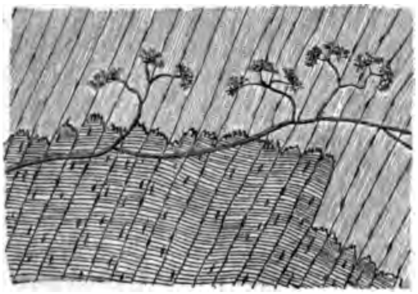


Two muscular fibres from the psoas of a guinea pig showing the terminations of the nerves. a, b, the primitive fibres with their transition into the terminal plates, P. P. Note neurilemma with nuclei continuous with the sarcolemma. Note nuclei in muscle. (After McKendrick.)

Each sarcomere then is occupied by dark and light matter. The dark matter seems to be more solid than the light matter. It is made up of several sarcous elements. From Fig. 38 one cannot see just how the matter of the sarcomere is disposed, but an end view (Fig. 39, B) shows it to be porous and that the white matter takes the form of cylindric extensions which fill the pores. Halliburton looks upon the sarcous elements as representing spongioplasm and the clear substance as representing the hyaloplasm (cytolymph).

The blood supply of the muscle is distributed as fine capillaries which occupy spaces between the fibres, but never pierce the sarcolemma. The nerves, however, terminate in end plates which lie within the sarcolemma. (See Fig. 40.) There are nerve endings in the tendons also. These nerves are sensory nerves and are stimulated by sudden change of tension upon the tendon. Fig. 41 shows this as well as the way in which the muscle fibres pass into tendon fibres.

FIG. 41

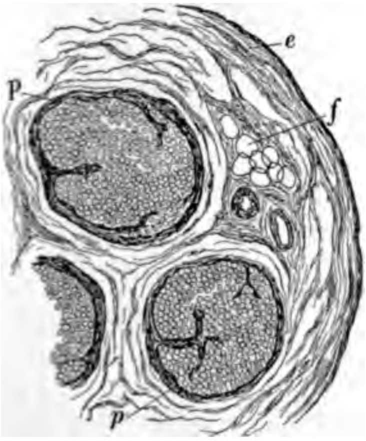


Nerve endings in tendon.

2. THE STRUCTURE OF NERVES.

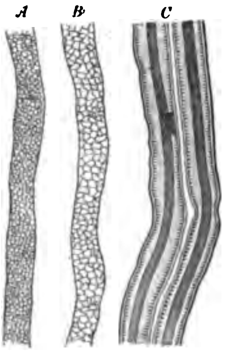
A *nerve trunk*, such as one finds in his dissections, is constructed as shown in Fig. 42, with a loose connective-tissue sheath (epineurium)

FIG. 42



Section of portion of a nerve trunk including three bundles, or funiculi, surrounded by the perineurium (*p*); the funiculi, together with the blood-vessels and adipose tissue, are united by the more general epineurium (*e*); the sections of the individual nerve fibres are held in place by the endoneurium; *f*, fat-cells, near which are the sections of bloodvessels. (After Piersol.)

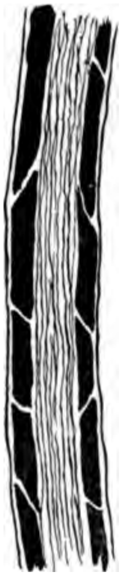
FIG. 43



Medullated nerve fibres: *A* and *B*, surface views of sheath and white substance of Schwann; *C*, optical section, showing fibrillated structure of the axis cylinder.

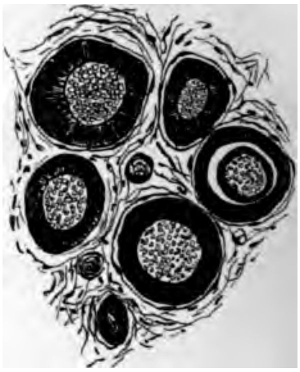
surrounding and separating the *nerve bundles.* Each bundle is ensheathed in *perineurium,* which sends extensions of *endoneurium* into each bundle. The bundles consist essentially of a great number of nerve fibres. A medullated nerve fibre (Fig. 43) is composed essentially of an axis cylinder surrounded by the medullary sheath or white substance of Schwann, which is in turn enclosed in the primitive sheath. The axis cylinder is composed in turn of fibrillæ. (See Fig. 44.) The fibrils seem to be separated by a ground substance as shown in Fig. 45.

FIG. 44



Axis cylinder, highly magnified, showing the fibrils composing it.

FIG. 45



Section across five nerve fibres (× 1000). The nerve was hardened in picric acid and stained with picrocarmine. The radial striation of the medullary sheath is very apparent. In one fibre the rays are broken by shrinkage of the axis cylinder. The fibrils of the axis cylinder appear tubular.

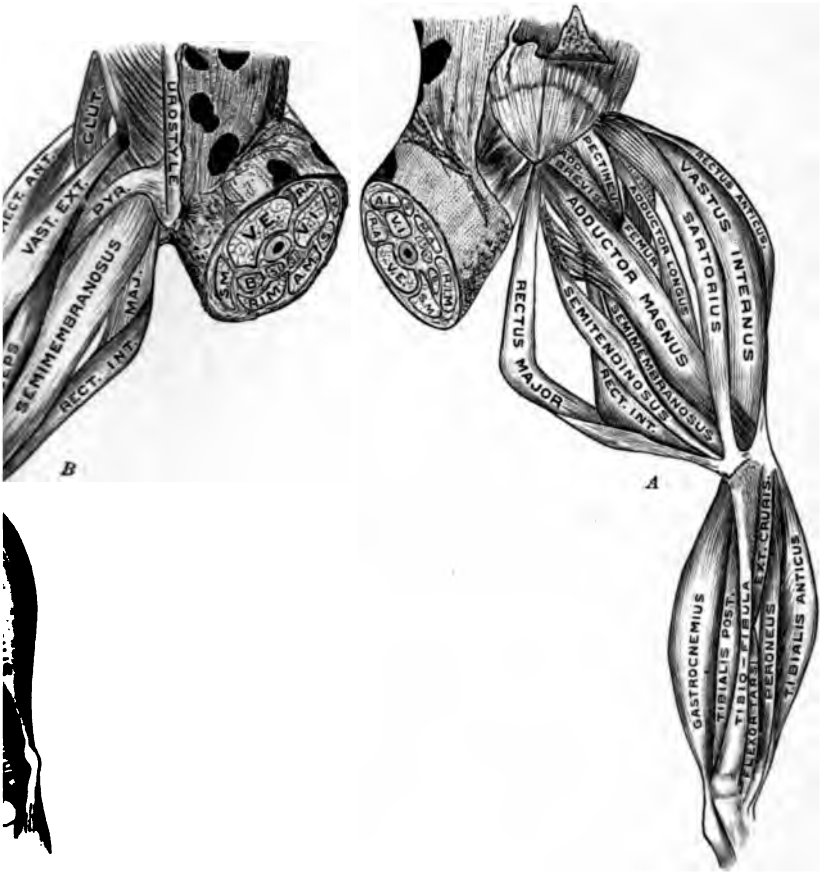
3. THE MUSCLE-NERVE PREPARATION.

The general principles of the physiology of contractile and irritable tissues are universally demonstrated with the tissues of a frog. Various muscles and nerves are used for these experiments, but the one most used is the gastrocnemius muscle with the sciatic nerve which supplies it.

Fig. 46 shows the anatomy of the frog's leg.

To make a muscle-nerve preparation one destroys the brain of the frog (piths it), pins it, dorsum upward, upon a cork board and removes the skin from the leg, thigh, and pelvic region. If the small, glistening tendon of the biceps be severed, where it is inserted upon the tibia, and the muscle dissected out and removed, one will find below where it lay the large trunk of the sciatic nerve with the accompanying bloodvessels—sciatic artery and sciatic and femoral veins. If the urostyle be removed the sciatic plexus will be revealed so that

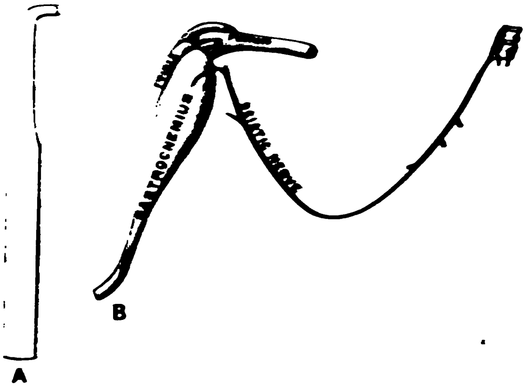
FIG. 46



Showing anatomy of the frog's leg: *A*, ventral; *B*, dorsal view.

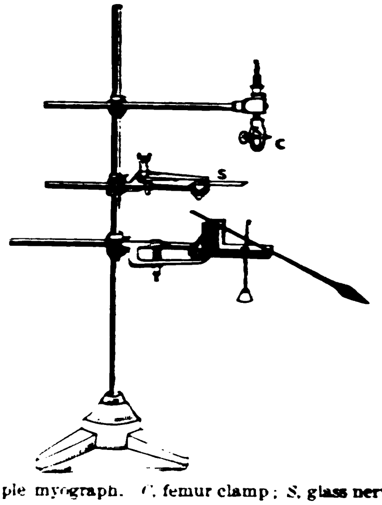
gently lifting the nerve with a fine glass rod it may be easily isected out from its spinal origin to the gastrocnemius. The rest the dissection required to produce the preparation as shown in g. 47 is readily made; the femur may be clamped to a support d the tendon attached to the lever of a myograph through a hook thread. (See Fig. 48.) Contraction of the muscle will raise the

Fig. 47



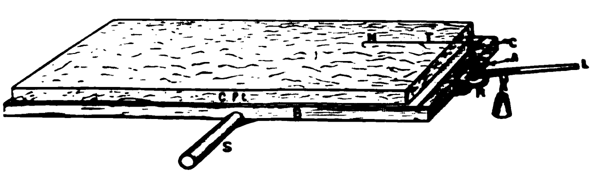
A. glass nerve hook for lifting a nerve while dissecting it out; *B*, muscle-nerve preparation as it appears when completed.

Fig. 48



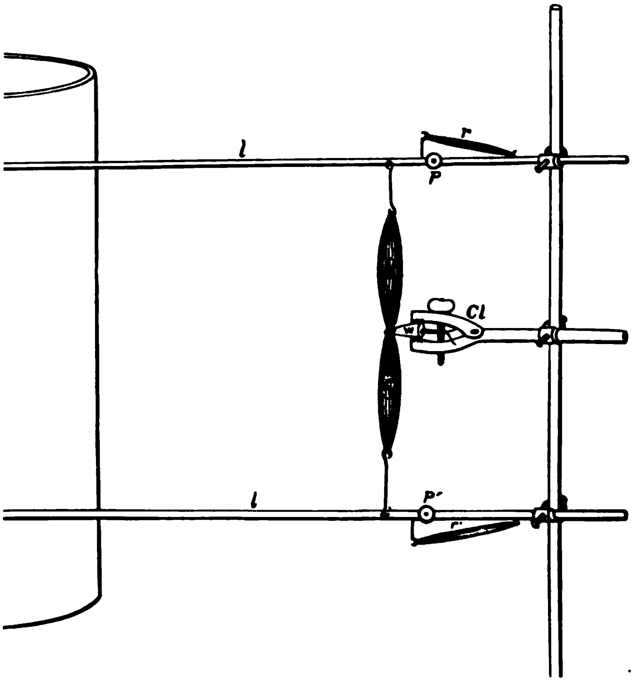
The simple myograph. *C*, femur clamp; *S*, glass nerve-rest.

Fig. 49



Frog-board myograph: *S*, the shaft which is clamped to the upright stand; *B*, the oaken base; *C Pt*, the cork plate to which the frog is fixed; *A*, the lever axis and slide lever holder; *W*, the weight; *L*, the light lever, about 20 cm. in length; *N*, the tendon hook which is joined through the thread *T*, which passed through the eye and under spring the catch (*e*); *R*, the lever rest.

FIG. 50



aph : *Cl*, femur clamp holding a wooden wedge (*W*), through which a loop of
The sartorius muscle (*S*) is held tightly by the loop of thread which encircles its
o tendinous extremities of the sartorius are hooked to the two levers *l l*. The
voted at *P* and *P'*. The muscle is put on a stretch by the two rubber bands
acing points *T* and *T'* are adjusted to a vertical line on the kymograph (*k*).

he latter may be made to trace its movements graphically
ating cylinder or kymograph.

IE PHYSIOLOGY OF MUSCLE AND NERVE.

ollowing brief summary of electrophysiology facts and
of fundamental importance only will be presented—
may be utilized in subsequent work in physiology,
gy, electrodiagnosis, and electrotherapeutics.

1. STIMULI.

e is dissecting out a muscle-nerve preparation he is
notice several muscular contractions, caused usually by
g of the nerve or of some of its branches, or by various

conditions present during the preparation. If one mount the preparation in the myograph, letting the nerve rest upon the glass slide, he may further test the effect of mechanical stimuli. The muscle responds when the nerve is severed with knife or scissors; it responds if it is pinched with forceps or pricked with a needle. If the muscle is exposed to the atmosphere it will begin after a time to contract rather spasmodically when there is no apparent stimulus; the contractions increase in extent and frequency until the muscle is practically tetanized. What has been taking place? The dry atmosphere has taken up the water from the tissue plasma, leaving the salts in concentrated solution; these salts may have caused the contractions of the muscles. Apply a strong solution of common salt to the nerve of a fresh preparation, and it will begin, almost at once, a series of contractions quite like those described above, producing a "salt tetanus." By applying glycerin to a fresh nerve a similar result is obtained. Such stimuli are called chemical stimuli.

If a fresh nerve be touched with a hot wire a response is elicited from the muscle. Temperatures between 0° C. and 100° C. do not produce contractions of the muscle unless there is a sudden change from one of the extremes to the other. Extreme temperatures only are efficient stimuli.

If while dissecting out a muscle-nerve preparation with a silver probe and steel scissors one touch the two instruments together when both are in contact with the tissues of the frog a vigorous contraction will be observed. The conditions were such as to cause the passage of an electric current from one metal to the other through the tissues of the frog. The tissues responded to the stimulus with a contraction. Mount the preparation and lay the nerve across the electrodes of a Daniell cell. Every time the circuit is "made" with the contact key the muscle contracts; every time the circuit is "broken" the muscle contracts, but it does not usually contract during the passage of a current. These stimuli have all been applied to the nerve (indirect stimulation); one may apply the same stimuli to the muscle itself[1] (direct stimulation), and will elicit a response in most cases, though it soon becomes evident that the muscle is not as sensitive to the various stimuli as the nerve is. In the case of the glycerin the muscle does not respond at all.

An important law of electrophysiology may be readily demonstrated at this point. If a curarized sartorius muscle be ligatured in the middle tightly enough to sever the muscle substance, but leave the connective tissue intact, and if this muscle be fixed in the middle, leaving the two ends free to fasten to levers, one can stimulate the two segments of the muscle and note the effect of the two poles, *anode* and *kathode*. Non-polarizable electrodes should be used for

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[1] First paralyze the nerve endings of the muscle by curarizing the frog.

this purpose, and one electrode should touch each segment of the muscle. If one segment contracts on make, it is the kathode segment; if only one segment contracts on break, it is the anode segment. Reverse the current with Pohl's commutator and the same is true—the make contraction is kathodic and the break contraction anodic. If both contract on making the current, the kathode segment begins first; if both contract on break the anodic segment begins first. The following laws of response to electric stimuli may be formulated: *Law I. The make stimulus is kathodic; the break stimulus is anodic. Law II. The "make" or kathodic stimulus of a current is more irritating to nerve or muscle than the "break" or anodic stimulus.*

A question which naturally arises very early in the study of various stimuli is: Does the way in which a given stimulus is applied to a nerve affect the response which the muscle gives? If one gently tap a nerve which is lying upon a glass plate, a slight contraction of the muscle will follow. A somewhat harder tap will cause a somewhat more vigorous response, but the maximum response is soon elicited. After that any increase in the strength of the stimulus will not cause an increase in the response. In a similar way a very weak electric stimulus will cause a weak response; a stronger stimulus, a stronger response, etc.; but the maximum response is elicited with what is really a very mild stimulus; beyond this maximum response any increase of stimulus will not elicit a greater response.

(I) *The stimulus of liminal intensity* is the weakest effective stimulus.

(II) *The stimulus of optimum intensity* is the weakest stimulus which will produce the maximum response.

Another way of varying the stimuli is to vary the time of application or the rate of change of conditions. One may sever or crush a nerve so slowly that the muscle will not respond. One may raise the temperature so slowly that the nerve may be cooked without having called forth a response. One may, through the Fleischl rheonom, send an electric current into a nerve so slowly that the muscle will not respond.

Summary.—(*a*) There are four kinds of stimuli: (I) mechanical; (II) chemical; (III) thermal; (IV) electric.

(*β*) Whatever stimulus be applied to a specialized sensitive tissue the response is the same in general character—*i. e.*, muscle always responds by contraction. (See page 52.)

(*γ*) The strength of the response may vary with the strength of the stimulus, but it is not at all proportional to the strength of the stimulus.

(*δ*) I. The stimulus of liminal intensity is the weakest effective stimulus.

II. The stimulus of optimum intensity is the weakest stimulus which will produce the maximum response.

(ε) I. The make stimulus is kathodic; the break stimulus is anodic. II. The kathodic stimulus is more irritating to nerve or muscle than the anodic stimnlus.

2. CHANGES WHICH TAKE PLACE IN A MUSCLE IN RESPONSE TO STIMULI.

After having watched the response of muscle tissue to the stimuli discussed in the preceding section the following facts must have become evident: (I) Muscle tissue is irritable. (II) Nerve tissue is irritable. (III) Muscle tissue transmits a stimulus from one part of a muscle to another; it therefore possesses the power of conductivity. (IV) Nerve tissue possesses the power of conductivity. (V) In response to stimulus a muscle changes its form.

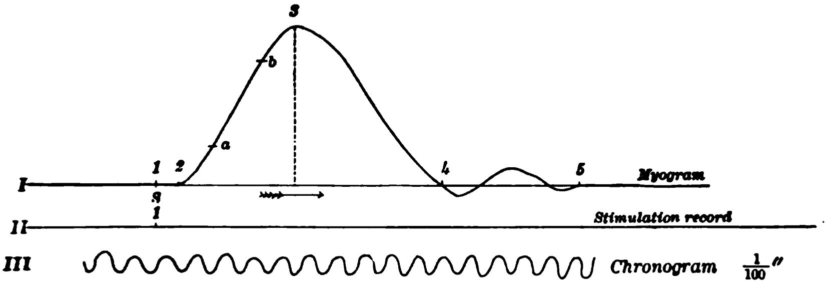
In the light of the experiments and discussions which have preceded, one may form a general conception of what takes place in contractile and irritable tissues in response to a stimulus. (I) Some internal change occurs in the nerve at the point where the stimulus is applied; this internal change is the invisible manifestation of the irritability of the nervous tissue. (II) The internal change begun at the point of stimulation is propagated along the nerve trunk; indeed, along the axis cylinders, because the nerve loses its insulating sheath before it reaches its final distribution. (III) It is transmitted to the individual muscle fibres through the end plates of the nerves which lie just within the sarcolemma of each fibre. (IV) It is propagated through the contractile substance of the fibre, so that all the fibres of the muscle contract at practically the same time. (V) There are internal changes in the muscle and nerve, which accompany the more evident *change of form* which takes place in the muscle. (VI) These internal changes are: *chemical*, *thermal*, and *electric*, as subsequent observation will demonstrate.

a. Change in Form.

1. **Change in Length.**—In studying the change in form which a muscle undergoes incident to its response to a stimulus it is customary to mount a muscle-nerve preparation in a myograph whose lever traces upon a kymograph any changes in length which the muscle may undergo. Almost any efficient stimulus may be used; the only requirement being that in its application to the nerve it must be sudden in its beginning, instantaneous in its duration, and sudden in its cessation. It is impossible to fill these requirements with chemical or thermal stimuli; but possible to do so with various mechanical and electric stimuli. It is customary to use electric stimuli. The "break" induction shock is especially adapted to this purpose.

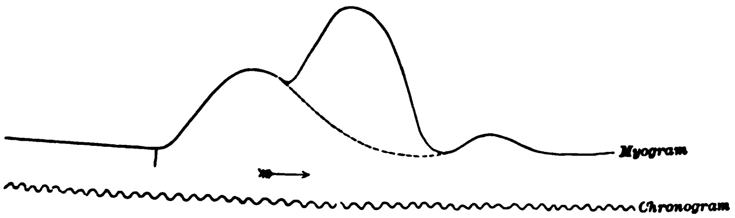
(*a*) **As the Result of One Shock** the muscle in contraction will trace upon a rapidly moving surface such a curve as is shown in Fig. 51. Such a tracing of a single muscular contraction reveals certain important facts regarding the response of a muscle to a stimulus. (I) On abscissa *II* (*s*) indicates the time of stimulation. Note that muscle, whose lever was tracing abscissa *I*, did not begin to shorten until about $\frac{1}{100}$ of a second had elapsed. This is called the *latent period*. (II) The period of contraction shows a slight acceleration at first, followed by a period of maximum rate of shortening (between *a* and *b*), after which there is a retardation of the rate of shortening until at 3 the apex of the curve is reached and for an instant retains this position of maximum contraction. (III) The period of relaxation follows immediately, but the rate of relaxation is less rapid at the beginning of this period than toward the end. Note that the period of relaxation (3 to 4) is longer than the period of contraction. (IV) If the muscle is moderately loaded and the lever without a rest or stop, the muscle will relax beyond its original position of rest; that is, the curve will pass below the abscissa, but will instantly recover itself coming above the abscissa. This is simply an after-effect due to the elasticity of the muscle and to the general conditions to which it is subjected.

FIG. 51



Tracing of single muscular contraction: 1 to 2, latent period; 2 to 3, period of contraction; 3 to 4, period of relaxation; 4 to 5, period of elastic after-effect.

FIG. 52

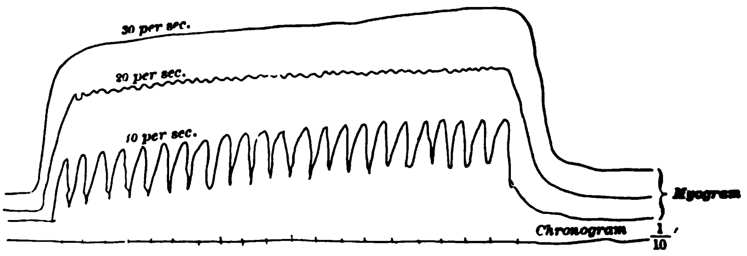


Tracing of a double muscle curve. (Foster.)

(*b*) Suppose a muscle be given a **Second Stimulus** before it has had time to complete its response to the first, what will the result be? Fig. 52 shows the typical result as traced by Foster. (I) Note that the crest of the second wave is higher than that of the first. (II) The contraction of the second is more rapid and its relaxation more rapid than observed in the first contraction.

(*c*) **The Summation of the Effects of Stimuli** is well illustrated in Waller's figure (Fig. 53). With a comparatively slow-moving cylinder and stimuli given at the rate of 10 per second the lever will drop back nearly to the abscissa, to rise again with another stimulus. With 20 shocks per second the lever remains nearly stationary. With 30 shocks per second the lever traces a perfectly straight line. This is a tetanus of the muscle. Tetanus is a sustained contraction of a muscle caused by a series of rapidly repeated stimuli. One may voluntarily bring a muscle into a state of sustained contraction. Though one is not conscious of the process which is going on in the nerve and muscle, he may infer from the foregoing that during sustained contraction there is a series of rapidly repeated stimuli (*motor impulses*) passing from the central nervous system to the muscle. The greatest number of voluntary movements which one can make in a second is limited to 8 or 10. The observations of Schaefer and of von Kries show "that the graphic record of even the steadiest voluntary movement exhibits a tremor" of 8 to 12 vibrations per second. (Waller.)

FIG. 53



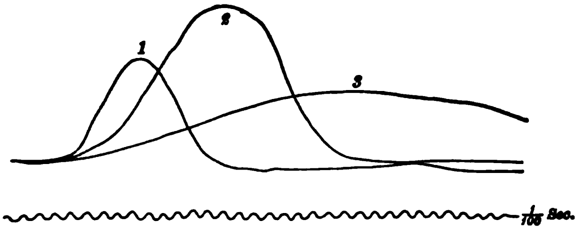
Summation of contractions; composition of tetanus. (After Waller)

It is generally accepted that in a sustained voluntary contraction the impulse frequency is about 10 per second. Involuntary contractions are slower in rhythm; the heart beat represents not a tetanic condition of the ventricles, but a "long twitch." Conclusive evidence of this is shown in the fact that only one change of electric condition occurs in the heart muscle at each contraction.

(*d*) **The Form of the Muscle Curve is Modified by the Temperature of the Muscle.**—When the temperature is only a little below normal the latent period is longer, the rise less sudden. When the temperature is very low the contraction and relaxation are both much prolonged and the shortening much less than normal. (See Fig. 54.)

(*e*) If a muscle be subjected to a **Series of Equal Stimuli at Short Intervals** (6 to 10 per second), each one of the first 10 or 12 contractions will be higher than the previous one, giving rise to the so-called "*staircase*" myogram. This seems to indicate that one response better fits the muscle for successive ones.

FIG. 54

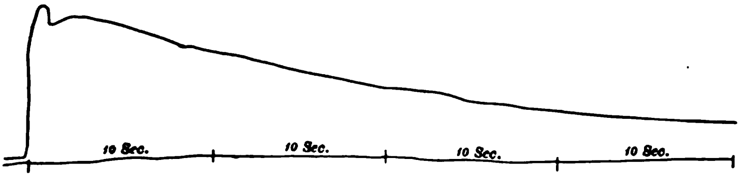


The effect of temperature upon muscular contraction: 1, normal; 2, cooling; 3, very cold. (Waller.)

(*f*) **The Muscle Curve is Modified by Drugs.**—Fig. 55 shows the effect of veratrin. Notice that though the contraction is about as sudden as usual the relaxation is much retarded—forty seconds not sufficing to bring the lever back to the abscissa.

(*g*) **The Muscle Curve is Modified by the Load** which the muscle must lift. A moderate load is likely to act as a supplementary stimulus to a muscle causing it to contract more with the load than without it; as the load is increased, however, two modifications may be noted in the myogram: (I) The latent period is longer because more time is required to generate sufficient energy to overcome the inertia of the load. (II) As the load increases the curve becomes progressively lower, though the actual work done may be greater.

FIG. 55



Effect of veratrin upon the myogram. (Waller.)

2. **Change in the Transverse Dimensions of the Muscle.**—The volume of the muscle remaining practically the same, there must be an increase in the transverse dimensions sufficient to compensate for the decrease in the length of the muscle. This thickening of the muscle may be recorded in two ways: (I) by resting the muscle on

a horizontal plate or within a shallow horizontal trough and resting a tracing lever upon its upper surface; (II) by clasping the muscle gently in a forceps lever and transmitting the movement through a pair of Marey tambours.

If one places a lever at each end of a long muscle like the sartorius it becomes at once evident not only that there is a thickening of the muscle during contraction, but that the thickening progresses as an undulation from one end of the muscle to the other when the muscle is stimulated at one end. The rate of propagation of this wave has been measured and is equal to from 1 to 3 metres per second, according to the various conditions of the experiment.

3. **The Work Done by a Contracting Muscle.**—The conditions under which most muscular contractions are studied, as outlined in the foregoing paragraphs, make it easy to estimate the work which the contracting muscle actually performs. Work done equals the product of the weight raised and the height through which it is raised. ($W = g \times h$.) If a muscle lift 100 gms. 5 mm. the work equals 50 gm.-cm. If a strong muscular contraction fail to lift a weight no work is done, though energy has been liberated in the muscle. If a loaded muscle be thrown into tetanus work is done only when the lever is raised, and not during the time when the weight is sustained. Energy is liberated, however, and the muscle is fatigued, but the energy does not take the form of mechanical work in the technical sense of that term.

The amount of work which a muscle can perform varies according to several factors.

(*a*) **Work is Modified by the Strength of the Stimulus.**—The weakest efficient stimulus—stimulus of *liminal intensity*—will cause a series of contractions lifting a given weight through a very short distance. Let the stimulus be gradually increased, the height of contraction will be rapidly increased to a maximum. The stimulus whose intensity is just great enough to cause the maximum contraction is called the stimulus of *optimum intensity*. Let the stimulus be increased; the contraction will not be greater; on the other hand, it is likely to be less because of fatigue from overstimulation.

(*b*) **Work is Modified by the Interval of Time** which elapses between the stimuli. The minimum interval, just short of a tetanic contraction, is unfavorable to the muscle because there is a rapid accumulation, within the muscle, of carbon dioxide, and other waste matter, which cause the rapid fatigue of the muscle. The optimum interval is such that the products of katabolism incident to the liberation of energy may be carried away from the muscle by the circulation. There can hardly be an optimum interval, then, for a muscle which has been removed from the organism. There is, however, an interval most favorable under the conditions, and that interval is from one to three or four seconds.

Work is Modified by the Load.—(*a*) *The disposition of the load:* a weight is simply hung upon the lever it stretches the muscle when the latter is at rest. The muscle under these conditions d to be "loaded," and it becomes quickly fatigued. (II) If ever comes to a rest at the end of the relaxation of the muscle is no stretching of the muscle between contractions. This lled "after-loading" a muscle. The short period of absolute e between contractions is advantageous to the muscle. (III) If eight is caught at the end of the contraction so that the muscle es without the load, it is found that the muscle can accomplish work than is possible under conditions (I) or (II). Fick was to introduce this modification of conditions of muscle work. instrument which he devised to accomplish it he called the k *adder*" (arbeit sammler).

) *The amount of the load* also modifies the amount of the work h a muscle is able to accomplish. A muscle will lift a hundred s as high as it will lift one gram, thus doing one hundred as much work in one contraction. The total work done in a of contractions leading to fatigue will be greater for medium gms. to 100 gms.) weights than for heavy weights (200 gms. to gms.), though the work of one contraction may be several times eat in the case of the heavier load.

) **Work is Modified also by the Dimensions of the Resting Muscle.** e extent of a contraction varies with the length of the con- ing fibres; while the strength of the contraction varies with the ber of the contracting fibres—*i. e.*, with the sectional area of nuscle. Both of the work factors ($g \times h$) are modified by the factors of the muscle volume; sectional area (a) and length (l); is, g varies as a, and h varies as l, therefore, $g \times h$ varies as l. Therefore, *the work which a muscle can accomplish varies e length multiplied by its sectional area*—i. e., *varies as its volume.*

iemical Changes which Take Place in a Contracting Muscle.

e chemical composition of dead mammalian muscle tissue is oximately as given in the following table:

Water		75 per cent.	to 77.5 per cent.
Solids		25 "	" 22.5 "
Nitrogenous		21 "	" 22 "
Proteid		18 "	" 20 "
Nitrogenous metabolites . Kreatin, xanthin, etc.	about	1 "	
Non-nitrogenous	about	0.5 "	" 1 "
Carbohydrates, dextrose . . .		0.5 "	" 1 "
Inorganic (carbonate and phosphate of K and Na)	about		1 "

e difficulty of determining just what chemical changes take in a living muscle incident to its activity must be evident.

The only index of these changes which present methods make possible is analysis of dead muscle that has been at rest and of dead muscle that has been fatigued just before being killed. Analysis of the gas consumed and given off by a resting or contracting muscle also affords data. From these various methods it has been conclusively determined that contracting muscle differs from resting muscle in producing: (I) more carbon dioxide, and (II) more nitrogenous waste matter; and in consuming: (I) more oxygen, and (II) more glycogen.

In this connection it is important to note that the muscle is chemically active when it is apparently at rest. Muscular tissue is the most important heat-producing tissue of the body. Heat production continues while the muscle is quiescent. This constant heat production is in part at the expense of the proteids of the muscle plasma (sarcoplasm) as well as of the proteids of the sarcous elements. The katabolism of these nitrogenous substances yields a series of nitrogenous katabolites, among which may be enumerated: kreatin, xanthin, glycin, and ammonium lactate.

The reaction of muscle changes with vigorous activity. Resting muscle is faintly alkaline because of the potassium and sodium carbonates and phosphates present. Accumulation of carbonic and possibly other acid in the muscle soon changes the reaction to a distinctly acid one.

The chemical changes which take place in muscle will be further discussed under Physiology of the Muscular System.

c. Thermal Changes which Take Place in a Contracting Muscle.

The chemical changes above enumerated are, in largest part, oxidations leading to the production of considerable quantities of H_2O and CO_2. But such changes are always accompanied by the evolution of heat not less surely in muscle than in a furnace. Vigorous and continued contractions produce considerable heat. One's impulse to be more active in cold than in warm weather is in response to the need of the organism for more heat. Heat is constantly liberated in muscle tissue, but more is liberated when the muscle is actively contracting than when at rest. This may be demonstrated by the use of thermoelectric couples, one set of which may be introduced into the gastrocnemius of one side, the other set into the other gastroc-

FIG. 56

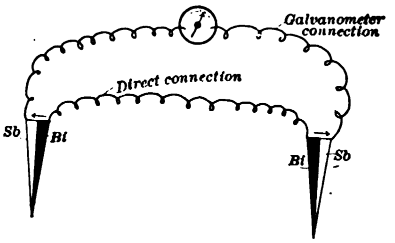


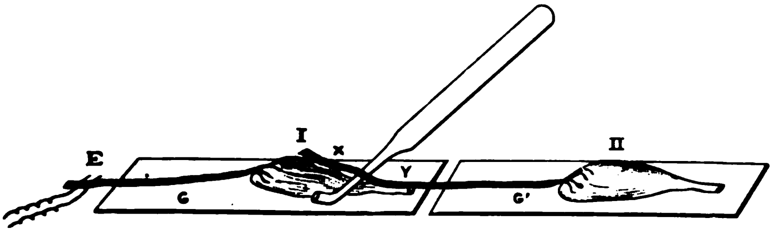
Diagram of thermoelectric couples. When both couples have the same temperature the galvanometer needle remains at rest.

nemius, while the long-connecting circuit passes to a galvanometer. (See Fig. 56.) Any increase in the temperature of the contracting muscle is indicated by a deflection of the galvanometer needle. This arrangement enables one to demonstrate the liberation of heat in contracting muscle. The second needle may be placed in a liquid whose temperature may be raised or lowered to bring the galvanometer needle to rest at the zero position; the temperature of the liquid may be determined by a delicate thermometer. Multiplication of the number of couples of needles makes the apparatus more delicate. Heidenhain gives the rise of temperature for one contraction of a frog's gastrocnemius as 0.001 to 0.005 or a degree Centigrade; and Helmholtz found a rise of temperature amounting to 0.14°–0.18° C. after two or three minutes of tetanization.

d. Electric Changes which Take Place in a Contracting Muscle.

In the process of dissecting out a muscle-nerve preparation one is likely to drop the cut-off central end of the sciatic nerve upon the gastrocnemius muscle. Should this occur a contraction of the muscle is almost sure to take place. Galvani performed this experiment and cited it as a proof that electricity exists in animal tissues. If one make two preparations and lay them upon glass plates, placing the nerve of preparation II upon the muscle of preparation I, so that it shall touch two well-separated regions, but not the intermediate portion of the muscle, the muscle of preparation II will contract when the contact is made, and it will probably repeat the contraction several times on subsequent contacts. Stimulate preparation I, the muscle of II contracts with every contraction of I. This is called a secondary contraction, and preparation II which contracts secondarily is called a *rheoscopic preparation* or a "*physiologic rheoscope.*" What is it in the cut-off nerve that causes a contraction of its muscle? What is it in a dissected-out muscle (I) that causes a contraction of a second preparation (II)? The stimulus which elicits a response from the rheoscopic preparation cannot be mechanical. It must be chemical, or thermal, or electric. If electric,

FIG. 57



one should be able to detect it through the use of the galvanometer or electrometer. Place upon the centre and end of a muscle contracting from mechanical stimulus, non-polarizable electrodes which are connected with a galvanometer or electrometer, and a deflection of the galvanometer needle or a change in position of the mercury meniscus of the electrometer demonstrates a difference of electric potential of the two regions of the muscle. This difference of electric potential was the stimulus which caused the secondary contraction of the rheoscopic preparation.

But the latter contracted also when touched to the resting muscle. It was once supposed that the difference of electric potential exists in all muscles at rest, and the terms "current of rest" and "current of action" were used. Hermann demonstrated, however, that a resting muscle when uninjured has no current and that injury induces a current in a general way proportional to the extent of the injury. The term "current of rest" then became misleading and was displaced by the term "*demarcation current*" or "*current of injury.*"

It has been found that: (I) *Normal muscle at rest is isoelectric*—*i. e.*, gives no evidence of a difference of electric potential in different regions. (II) *Local injury induces a difference of potential,* instantly indicated by the galvanometer or electrometer. (III) *Local action induces a difference of potential*, indicated by the galvanometer or electrometer. The current of a galvanic cell passes from the zinc plate to the copper plate—*i. e.*, from the plate where there is chemical action to the plate where there is no chemical action. The current of an injured muscle passes from the injured portion to the normal portion—*i. e.*, from the portion where there is much chemical action toward the portion where there is little chemical action.

FIG. 58

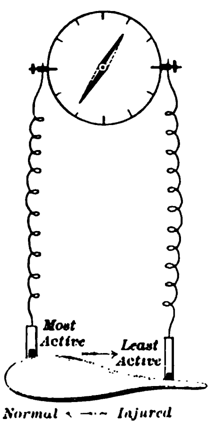


Diagram showing direction of the "current of injury" (<——) and of the "current of action" (——>). Also the "negative variation" of needle during action of injured muscle.

The current of action is, in the same way, from the portion most active to that least active.

Both of these factors may be at work at the same time—*i. e.*, an injured muscle may be made to contract. The current of injury passes through the galvanometer from the normal to the injured portion. The point of injury is the point of least activity—that is, the change from rest to action will be greater at the normal part. Therefore, the current of action will pass through the galvanometer from the injured to the normal. Thus stimulation of an injured muscle will cause the needle to swing back toward the opposite direction. This phenomenon is called the *negative variation*. These relations are represented diagrammatically in Fig. 58.

If the electrodes be placed one upon the base and one upon the apex of the ventricle of the heart, there will follow a double variation with each heart cycle. In the first phase of the cycle the base is electronegative to the apex, in the second phase of the cycle the apex is electronegative to the base, thus leading to the term "diphasic variation" of the heart.

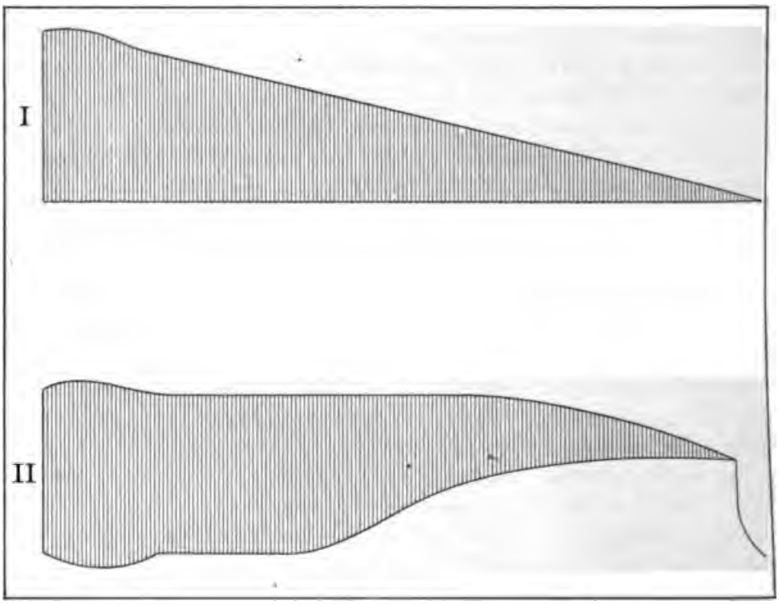
In this connection it may be stated that all active tissues manifest the presence of difference of potential in different regions. For example, the outer surface of the hand is negative to the inner surface; the fundus of a gland is negative to the hilus; the optic nerve is negative to the cornea, etc.

e. **Fatigue.**

In response to various stimuli muscle tissue undergoes changes in *form*, in *temperature*, in *electric* condition, all of these forms of energy being liberated through the *chemical* changes which accompany them. Mention has been made above of the accumulation in the muscle of the products of the chemical changes; also of the gradual decrease in the height of successive contractions after the muscle has been contracting many times. These two phenomena are the distinctive phenomena of fatigue and the first is the cause of the second. The accumulation of the products of chemical action is the cause of the progressively decreasing power of the muscle.

The decreasing power of the muscle manifests itself by a decreasing height of the contraction waves. Just at first the waves may increase in height—the *staircase contractions*. Following this there will be a number of waves of nearly the same length; finally the waves begin to shorten up until there is no response to the recurring stimuli. Then the muscle is said to be fatigued. The conformation of the series of fatigue waves will vary considerably with the way in which the load is disposed. Fig. 59, *I*, shows a typical fatigue tracing from an "after-loaded" muscle, while *II* shows that from a "loaded" muscle. In the latter the stretching during the period of rest irritates the muscle and brings it finally into a state of typical tetanus. The fatigue is postponed by using the optimum strength of stimulus—the optimum rate and a medium load. If a fatigued muscle is given a few moments' respite or rest it recovers in part and will respond vigorously to subsequent stimulation, but tires very quickly again. A muscle which is in its normal situation, receiving the benefit of exchange of material through the circulation, will accomplish much more work before fatiguing than will be the case with an excised muscle. Furthermore, the intact muscle will recover in a short time, while the excised muscle makes only a moderate recovery through the removal of CO_2 by diffusion. Fatigue is accompanied by a decrease of extensibility and elasticity; in common words, *fatigue is accompanied by stiffness.*

FIG. 59



Showing the effect of disposition of the load on the contraction of muscles, modifying the amount of work done.

f. Rigor.

After the death of a muscle it undergoes certain changes which are similar to those which take place during fatigue—namely, the accumulation of CO_2 and of sarcolactic acid. Accompanying these chemical changes there is the "stiffness of death"—*rigor mortis*—due to the coagulation of the myosin. If fresh muscle substance be coagulated by heat—50° to 60° C.—there will also be a formation of CO_2 and other katabolites, accompanied by the "stiffening of heat," or *rigor caloris.* The three conditions—viz., fatigue rigor, rigor mortis, and rigor caloris—are closely related, both physically and chemically.

3. THE RELATION OF THE NERVE TO VARIOUS STIMULI.

The living nerve in its normal position in the animal body functions as a conductor of impulses. These impulses may arise in the central nervous system and be conducted to various peripheral organs; or they may arise in various peripheral (sense) organs and be conducted to the central nervous system. In either case the nerve neither adds to nor subtracts from the original impulse which it receives, but transmits it along the course of the nerve from one end to the other. Just how these impulses are transmitted is unknown. One can follow the steps of the chemical changes that are propagated along a fuse or of the physical changes that are propagated along a wire conductor of electricity, but the physical and chemical changes which are propagated along the axis cylinder of a nerve are still unknown quantities as to their exact nature. It is generally accepted that they are ultimately chemical and that the initiatory chemical (metabolic) changes are accompanied by electric changes, probably also by thermal changes.

a. The Properties of Nerve Trunks.

The fundamental and essential property of a nerve trunk is conductivity. The experiments which are described above make it evident that a nerve trunk is not only a conductor of an impulse, but that a stimulus in any part of its course may start at that point a change which will be propagated, apparently in a perfectly normal way, to the normal terminus of the nerve, and there transmitted to the structures normally receiving impulses from the nerve. For example, an injury or an electric shock to the sciatic nerve sets into operation at the point of the stimulus a change which is propagated to the muscles supplied by the nerve, and these structures give the normal response to the impulse. The second property of a nerve is irritability or excitability.

b. Conductivity.

The rate of propagation of an impulse along a nerve may be determined by stimulating a nerve near to its muscle, or five or six centimetres farther away from the muscle. The response to the stimulus must be recorded upon a rapidly moving surface, such as the spring myograph, and the time in hundredths of a second must be recorded upon the same surface by a tuning fork (Fig. 33). The difference in time elapsing between stimulus and response in the two cases is the time required to traverse the five or six centimetres of extra nerve. In this way the rate of propagation or conduction may be determined. This method of experimentation has given the following results: Helmholtz found the rate of transmission in the motor nerves of a frog to be 27 m. per second. The rate of conduction in sensory nerves is about 35 m. per second.

The conductivity of a nerve is decreased by low temperature and increased by high temperature.

The conductivity may be destroyed by the direct application of alcohol or ether to the nerve trunk, while its irritability will not be much affected. "Carbon dioxide may destroy the irritability, though leaving the conductivity unimpaired." (Lombard.)

A strong constant current decreases the conductivity of a nerve in the region of the anode during the passage of the current and in the region of the kathode after removal of the current. This modification of conductivity may be called *Law III.* of electrotonus; *Laws I.* and *II.* were given above.

c. Irritability.

If a constant current traverse a nerve, entering and leaving by non-polarizable electrodes, the nerve will be thrown into a state called *electrotonus.* The condition of electrotonus is characterized by a moderate change in conductivity, mentioned above, and a profound change in irritability. The irritability of the nerve is increased in the region of the kathode and decreased in the region of the anode. In Fig. 60 the line *A* to *B* may serve for both nerve and abscissa. The curve *I* to *I′* indicates the degree of irritability; note that the irritability is increased in the region of the kathode and decreased in the region of the anode. It indicates also that the influence of the two electrodes decreases as the distance from the pole increases; and that in the intrapolar region there is a neutral area where the irritability is neither increased nor decreased. The region of decreased irritability in the neighborhood of the anode is said to be in a condition of *anelectrotonus;* the region of increased irritability in the neighborhood of the kathode is said to be in a condition of *katelectrotonus.* The change in irritability manifests itself when a stimulus is applied to the nerve in the region of anelectrotonus or of katelectrotonus. Arrange the apparatus as indicated in the diagram (Fig. 61). Through the agency of commutator *C* one can make either electrode the kathode by reversing the current.

FIG. 60

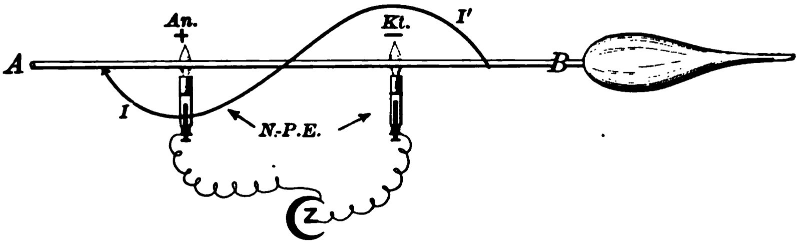
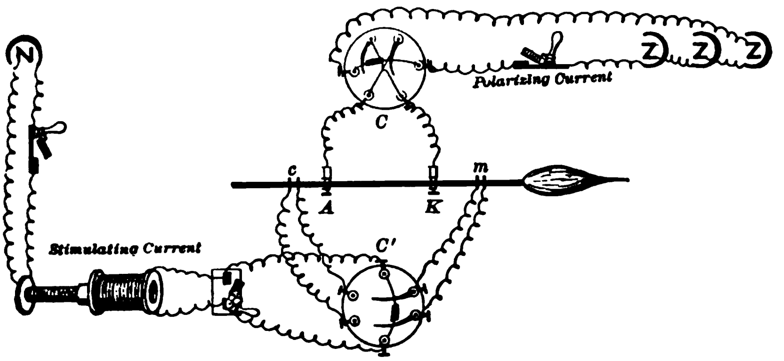


Diagram illustrating electrotonus. *N.-P.E.*, non-polarizable electrodes; *An.*, anode; *Kt.*, kathode; *I, I′*, curve illustrating degree of irritability—decreased in the region of the anode and increased in the region of the kathode.

Through commutator C' one can throw the stimulus at *m*, the muscular end of the nerve, or at *c*, the central end of the nerve. Arrange the apparatus so that the kathode is near the muscle as indicated in the figure. Before "making" the constant or "polarizing" current stimulate with the induced current at *m* or *c*, using a "break shock" that will cause a moderate contraction—*i. e.*, bring the secondary coil just inside the minimum limit of stimulation. Turn on the polarizing current after a few moments, stimulate at *m*, in the katelectrotonic region; the response will be noticeably greater than the normal. Stimulate at *c* in the anelectrotonic region; the response will be noticeably less than the normal. Reverse the direction of the polarizing current, bringing the anode nearer to the muscle. The region which before was in a condition of katelectrotonus is now in a condition of anelectrotonus and conversely. Stimulate in the region *m* and the response will now be less than normal because the irritability of the nerve has been decreased in the region of the anode, in the region of anelectrotonus. On the other hand, the response at *c* will be greater than normal because of the influence of the kathode, inducing a state of katelectrotonus. These facts are summed up in a law of electrotonus:

FIG. 61



Arrangement of apparatus for demonstrating electrotonus.

LAW IV. *The passage of a constant current through a nerve modifies its irritability, increasing it in the region of the kathode* (state of katelectrotonus) *and decreasing it in the region of the anode* (state of anelectrotonus).

d. Pflueger's Law of Contraction.

If one stimulate the nerve of a muscle-nerve preparation, and note visually or graphically the response which the muscle gives, he will find that with uniform and favorable conditions the preparation will respond in a uniform way to a varying stimulus. The stimulus should be varied in two ways: (I) as to direction; (II) as to strength. If the current pass along the nerve toward the muscle—*i. e.*, the kathode being placed nearer to the muscle—the current is called a "*descending*" one; if the anode is nearer to the muscle the current is called an "*ascending*" one.

To vary the strength of a current one should use either a simple rheocord or a Du Bois-Reymond rheocord, so that the strength may be varied by infinitesimal increments. Non-polarizable electrodes are preferable, though platinum electrodes may be used with good results. Choose healthy, vigorous frogs; pith them two or three hours before they are to be used. Protect the preparation against rapid drying by mounting it in a moist chamber. With all conditions favorable the results will be as follows: A very weak descending current will affect the muscle first, causing a slight contraction on *make*. With a somewhat stronger current there will be a contraction *on make of both ascending and descending currents.* A further increase in the strength of current will call forth a response *on both make and break of both ascending and descending currents.* As the current is gradually increased from this point it will be noted that the contractions are not equal in extent; some are stronger and some are weaker; the weaker ones finally drop out and the stronger ones increase in strength. These strong contractions occur *on the make of the descending current and on the break of the ascending current.* The results may be thus tabulated:

Current.	Descending.		Ascending.	
	Make.	Break.	Make.	Break.
Weak	Contract.	Rest.	Contract.	Rest.
Medium	C	C	C	C
Strong	C	R	R	C

It now becomes necessary to account for these results, using the laws which have been formulated. To that end let us here present the laws again.

Law I. *The make stimulus is kathodic (KMC); the break stimulus is anodic (ABC).*

Law II. *The make or kathodic stimulus of a current is more irritating to nerve or muscle than the break or anodic stimulus.*

Law III. *A strong constant current decreases the conductivity of a nerve in the region of the anode during the passage of the current and in the region of the kathode after removal of the current.*

Law IV. *The passage of a constant current through a nerve modifies its irritability, increasing it in the region of the kathode* (state of katelectrotonus) *and decreasing it in the region of the anode* (state of anelectrotonus).

The results tabulated above may be graphically represented as shown in the accompanying figure (Fig. 62).

Note that with a weak descending current there is a "kathodic make contraction" (*KMC*); that with a medium descending current there is both an "anodic break contraction" (*ABC*) and a "kathodic make contraction" (*KMC*). The other indicated results will be found to correspond to the table. Why is there a kathodic make contraction only, with a weak descending current? Because (I) the make contraction starts at the kathode (Law I); (II) there will be a kathodic contraction before there is an anodic contraction in accordance with Law II. These laws account also for the results obtained with an ascending current. With a medium current, kathodic make contraction is in response to Law I. The fact that there is an anodic break contraction indicates that in response to Law II the break stimulus has become sufficiently strong to cause a response. The same thing is true for both ascending and descending currents. In the case of a strong descending current we get a kathodic make contraction in response to Law I. In response to an anodic break stimulus there is no contraction because according to Law III the conductivity is decreased in the region of the kathode at the moment of the break of a strong current. At the make of a strong ascending current there is no response, though there has been a strong kathodic stimulus because the conductivity of the nerve is much decreased in the region of the anode *during* the passage of the strong current (Law III). In this case the anodic break stimulus causes a contraction because the region of reduced kathodic conductivity is not between the stimulated point and the muscle.

FIG. 62

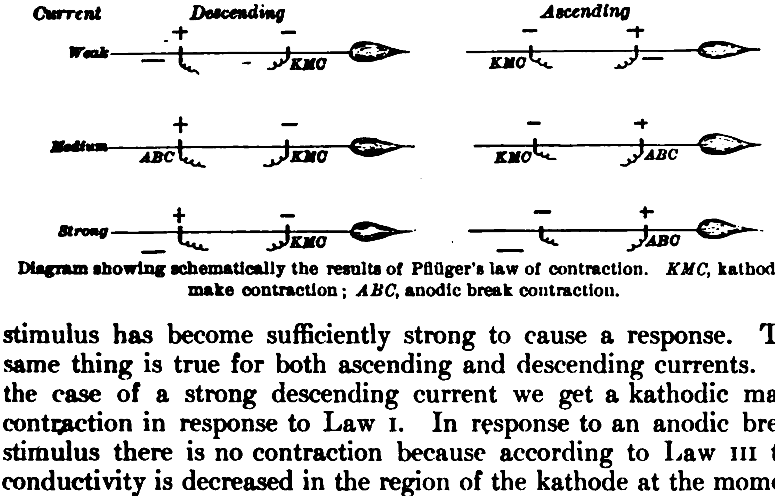
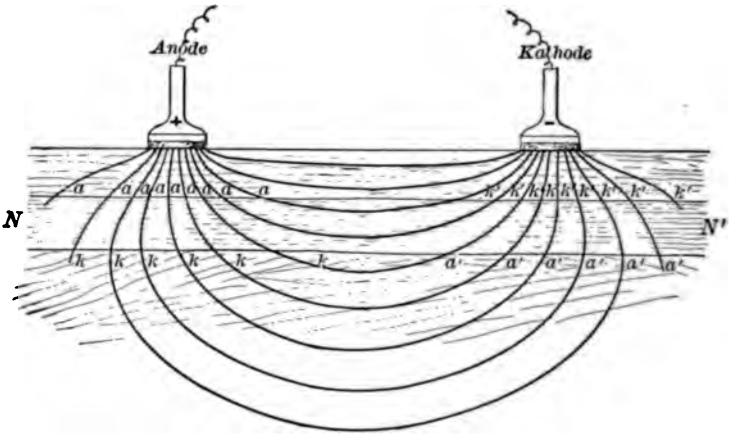


Diagram showing schematically the results of Pflüger's law of contraction. *KMC*, kathodic make contraction; *ABC*, anodic break contraction.

e. The Application of the Laws of Electrotonus.

In the application of the laws of electrotonus to the problems of electrodiagnosis or electrotherapeutics there are some complicating factors to consider. If the electrodes (usually metallic plates covered with chamois or sponge which is moistened when in use) are placed over the course of a nerve the current will diffuse widely through the tissues from the anode and converge again upon the kathode on leaving the tissues. (See Fig. 63.) Let N N' represent a nerve trunk, the current enters it at a a a, traversing it and leaving by k k k. As the current converges toward the kathode it traverses the nerve trunk again, entering it at a' a' a' and leaving at k' k' k'.

FIG. 63



Application of the laws of electrotonus.

But the point where a current enters a nerve is called the anode, and the point where it leaves, the kathode. This leads to the differentiation of four physiologic poles, while there are only two physical poles.

(I) The physiologic anode under the physical anode (a, a, etc.).
(II) The physiologic kathode under the physical anode (k, k, etc.).
(III) The physiologic anode under the physical kathode (a', a', etc.).
(IV) The physiologic kathode under the physical kathode (k', k', etc.).

A contraction caused by the influence of the current at the physiologic kathode under the physical anode is called an anodic make contraction (*AMC*). A contraction caused by the influence of the current at the physiologic anode under the physical anode is called anodic break contraction (*ABC*). In a similar way there may be a kathodic make contraction (*KMC*), and a kathodic break contraction (*KBC*).

It is important to determine which of these various stimuli will be most effective. In addition to the above laws of electrotonus one will need to apply a fifth law.

Law v. *The denser the current, all other things being equal, the stronger the stimulus.* In the figure note that the current is denser at the physiologic anode under the physical anode than at the physiologic kathode under the physical anode.

The kathodic make contraction is stronger than the anodic break contraction.

$$(1)\quad KMC > ABC.$$

This is in accordance with Laws I and II, Law V not applying here because the density is the same, providing the nerve is equally near the surface under the two poles. For similar reasons, *the anodic make contraction is stronger than the kathodic break contraction.*

$$(2)\quad AMC > KBC.$$

If KMC is greater than ABC and if AMC is greater than KBC we may conclude that:

$$(3)\quad KMC + AMC > ABC + KBC,$$

or *the sum of the make stimuli must be greater than the sum of the break stimuli;* in consequence of this, *the contraction which occurs at make* (in response to the double stimulus) *is greater than the contraction which occurs at break* (in response to the double stimulus).

The anodic make contraction (AMC) *may or may not be stronger than the anodic break contraction* (ABC)—*i. e.:*

$$(4)\quad AMC > ABC \text{ or } AMC < ABC.$$

In this case we have the stronger effect at the physiologic kathode (Law I) to offset the greater density of the current at the physiologic anode (Law V); one may be stronger than the other, but the difference is at most slight.

We are now in a position to understand what will take place when the current is progressively increased from weak to strong. The results may be thus tabulated:

Weak Current	KMC			
Medium Current . . .	KMC	AMC	ABC	
Strong Current	KMC	AMC	ABC	KBC

The above table gives the normal reaction. *If degeneration has made some progress the weak current elicits the anodic make contraction* (AMC) *before it does the kathodic make contraction* (KMC), an important fact in electrodiagnosis.

B. THE GENERAL STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM.[1]

We have studied the way in which contractile and irritable tissues respond to certain external and artificial stimuli. Before we enter upon the special physiology of the various organs and systems of organs it will be profitable for us to consider briefly: (I) what relation nervous tissue bears to the organism as a whole; (II) whence come the various stimuli which influence the operation of the different organs and tissues of the body; (III) what tissues (besides contractile tissues) are influenced in their activity by the central nervous system.

1. GENERAL CONSTRUCTION OF THE NERVOUS SYSTEM AND ITS RELATION TO THE ORGANISM AS A WHOLE.

Though the tissue of the nervous system is disposed in prominent structures which may be called organs—*e. g.*, brain, spinal cord, etc. —these structures are not organs in the same sense that the lungs are organs belonging to the respiratory system. *The whole nervous system is really one organ.* This organ is composed of (I) a parenchymal tissue, which is the specialized tissue of the organ, endowed with a specialized function, and (II) a supporting tissue. As in other organs, so here the supporting tissue belongs to the connective-tissue series, the more delicate connective tissue of the deep-lying portions of the central nervous system being somewhat specialized and called neuroglia, while the remainder represents the more common forms of areolar, fibrous, and elastic connective tissues.

a. The Neurone.

The parenchymatous or active tissue of the nervous system is composed of nerve cells. The nerve cell is so highly specialized a structure that it has received the special name *Neurone.* The neurone is the unit of structure of the nervous system. *A neurone* (see Fig. 64) *consists of a neural cell body with all of its processes.*

The protoplasm of the cell body presents a delicate fibrillated structure. The fibrillæ seem to be continuous with those which constitute the one or two axis cylinders which are among the cell processes. Besides the fibrils, the cell protoplasm is more or less

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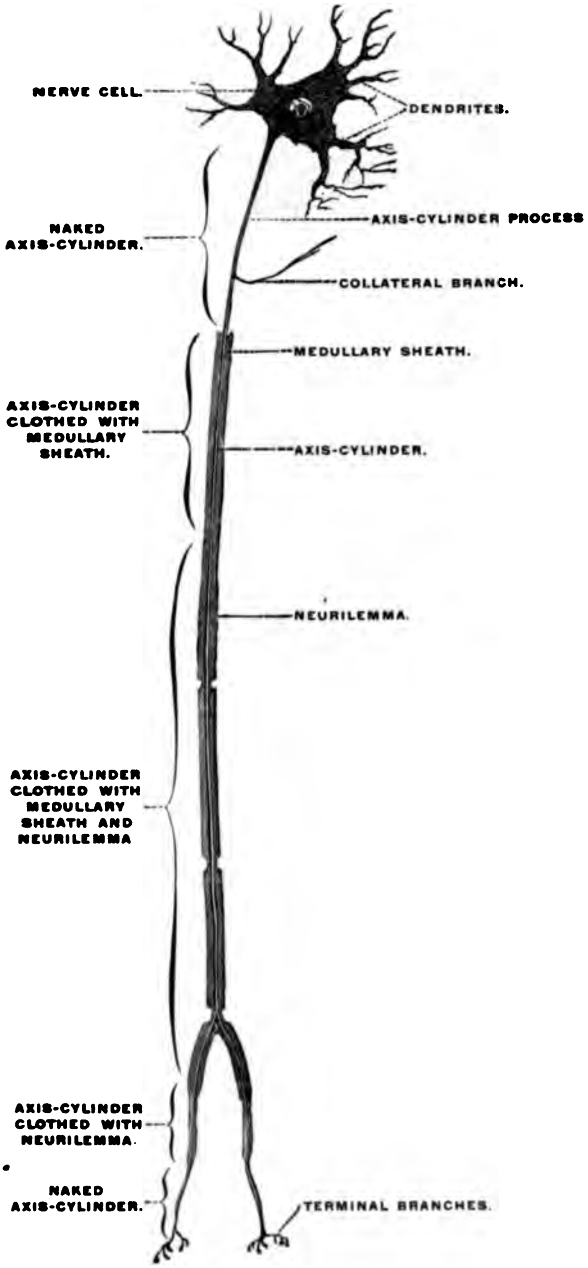
[1] The student is not in a position to comprehend the way in which the various systems of organs and tissues (circulatory system, respiratory system, digestive system, etc.) are governed, how they are influenced by outside conditions, and how one system exerts an influence upon another, unless he has at least a general idea of the construction of the nervous system and the functions of its various structures. It is the object of this section to give a brief outline of the most essential features of the nervous system.

FIG. 64



Schema of a neurone. (After Verworn.)

charged with fine, dark granules (chromophiles), which are important in the metabolism of the cell, increasing during periods of rest and decreasing during periods of activety. Occupying a fairly central position in the cell body is a relatively large nucleus, with a distinct nucleolus.

The cell processes are numerous and complex. As to structure they may be arranged in two classes: (I) The protoplasmic process —short and much branched, their tree-like appearance giving them the name *Dendrites*. (II) The axis-cylinder process, which is usually much elongated, little branched near the cell body, and usually insulated in a medullary sheath. As to function, cell processes either bring impulses to the cell body or they carry impulses away from it. Those which bring impulses to the cell body are called *afferent* cell processes, and those which carry impulses away are called *efferent* processes. The protoplasmic processes are without exception afferent.

If a cell has only one axis cylinder it is without exception efferent. If it has two, one of them is afferent and one efferent. These facts readily lead to confusion in the use of terms. To avoid this confusion the best authorities are now adopting a new term to represent the efferent process—the term NEURAXONE or *Neurite*, or *Axone*. As now understood *the term dendrite always refers to an afferent process. All neuraxones are axis cylinders structurally.* Most dendrites are protoplasmic processes, but some (the sensory nerves) have become modified into axis cylinders.

tr

b. Features of the Spinal Cord.

The nerve trunks with which one deals in the experiments in muscle-nerve physiology are really bundles of insulated axis cylinders. They normally carry motor impulses to the muscles from the cell body which they represent. But where is this cell body located? If one follow the nerve trunk he will find that just before reaching the central system it divides into two roots, an anterior (or ventral) root and a posterior (or dorsal) root. If the anterior root be stimulated one will observe the same response as if the trunk had been stimulated in the same way nearer to the muscle. If the posterior root be stimulated no such response will be observed.[1] One is justified in inferring that the neuraxones which he is tracing left the spinal cord by the anterior roots. A transverse section of the spinal cord should show the large cell bodies in the anterior gray horn. (See Fig. 65.) Note their numerous branches. In a few cases the neuraxones may be traced into the nerve bundles which make up the anterior root. From the accompanying diagram note that the motor neurone in question is in communication—through its dendrites: (I) with motor neurones from the brain and (II) with sensory neurones. (See Fig. 66.)

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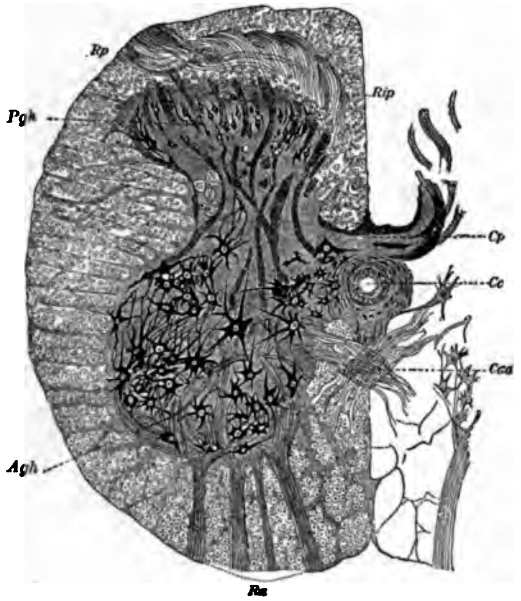
[1] There may be a general response, the nature of which will be explained later; but there will be no definite response of the particular muscles supplied by the motor nerve in question.

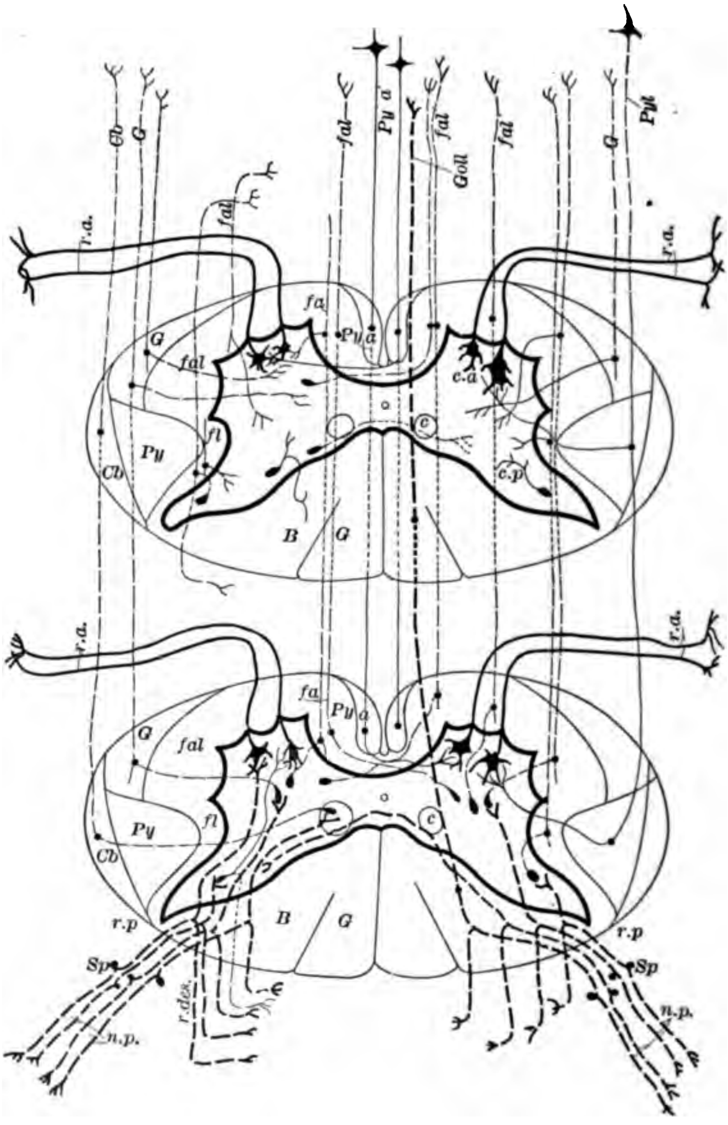
The motor neurone normally sends a motor impulse to the muscle which it supplies, only when it receives an impulse through its dendrites. From the connection which it has it is evident that it may receive such an impulse from one or the other of two sources: (I) from the brain; (II) from the sensory nerves. If the motor impulse originates in the brain it is sent through the central motor neurone to the peripheral motor neurone, thence through it to the muscle. Two neurones, two cells, are required to transmit an impulse from the brain to the peripheral organs. This holds good for secreting and excreting organs as well as for motor organs. But the peripheral motor neurone may be influenced by sensory neurones, by neurones which bring impulses to the central nervous system from the skin and various sensitive organs of the periphery. Note in the diagram that these peripheral sensory neurones (sensory neurones of the first order) enter the spinal cord by the posterior root, and that they communicate (I) either directly or indirectly with a motor neurone; (II)

FIG. 65



Half of a section through the lumbar cord. *Ra*, anterior root; *Rp*, posterior root; *Rip*, inner portion of the posterior root; *Cp*, posterior commissure; *Caa*, anterior commissure; *Cc*, central canal. The fine network of medullary fibres in the gray matter and the network of medullary fasciculi in the otherwise gray posterior commissure are not shown. *Agh*, anterior gray horn; *Pgh*, posterior gray horn. (Edinger, after Deiters.)

FIG. 66



Schematic representation of the course of the fibres in the spinal cord. I. **THE MOTOR TRACT** *a. Central neurone:* lateral pyramidal tract (*Py l*) and **anterior pyramidal tract (*Py a*); terminal** arborization in the anterior horn. *b. Peripheral neurone:* **anterior horn cells—anterior root** (*r. a.*)—motor nerve muscle. II. THE SENSORY TRACT. *A. Peripheral neurone:* **sensory nerve** (*n. p.*), spinal ganglion (*Sp*)—posterior root (*r. p.*) of the spinal cord. **In the posterior root zone of** the posterior columns each fibre divides into an **ascending and a descending branch (short and** long fibres. (*a*) *The short tracts* curve into the posterior horn as: 1. **Reflex collaterals to the** anterior horn, shorter reflex arc, longer reflex tracts **(intercalation of another neurone).** 2. **Fibres to the cells of the middle zone of the gray substance. 3. Fibres to the cells of Clarke's** either directly or indirectly with the brain. Note that a spinal ganglion (*Sp*) is located upon the posterior root. This ganglion of the posterior root is the location of the cell bodies of the peripheral sensory neurones. From the peripheral sense organ to the cell body in question the impulse is conducted along an afferent axis cylinder which is a modified dendrite. From the cell body the impulse is conducted into the spinal cord along an efferent axis cylinder or neuraxone. This neuraxone sends off collateral branches which communicate directly with peripheral motor neurones of the same segment, or indirectly with motor neurones of neighboring segments of the cord, or finally directly or indirectly with the brain through a central sensory neurone (or neurone of the second order).

2. GENERAL FUNCTIONS OF THE NERVOUS SYSTEM.

a. Reflex Action.

A careful study of these relations between the sensory and motor neurones makes it evident that the activity of any peripheral motor (or glandular) organ may be influenced in one or the other of two ways: (I) Through the direct influence of impulses entering the central system by the sensory neurones of the same (or neighboring) segment which furnishes the motor nerve supply; or (II) through the influence of the brain. The first method of influencing the activity of an organ is called reflex. Note that reflex action involves typically two neurones: the peripheral sensory neurones and the peripheral motor neurone. Reflex response to a stimulus, as when one jerks his hand from a hot object, is accomplished in the following manner; (I) The sensory nerve endings in the skin are stimulated by the hot object; (II) the stimulus starts a message or impulse along the afferent nerve to the cell body in the posterior root ganglion; (III) the cell

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columns (*c*). 4. Fibres to the central and especially the medial anterior horn cells (commissural cells). 5. Fibres to the posterior horn cells. (*b*) *The long tracts* (6) pass first into Burdach's column, higher also into Goll's column, and thus to the nuclei of the posterior columns in the medulla. (Here they join the fillet.) *B. The central neurone.* It begins with the cells of the terminal places of the peripheral, enumerated under 2 to 6. 1. From those which have been enumerated under 2 as "column cells" arise the fibres of the anterior ground bundle of the same side (*fal*) (*fl*) and the columns of Gowers (*G*). 2. From those mentioned under 3: the lateral cerebellar tract of the same side (*Cb*). 3. From those under 4: fibres which cross in the anterior commissure to the anterior lateral column (*fal*) (*fl*) to ascend in the other side. 4. From those under 5: fibres to the lateral limiting layer (*fl*) and to the ventral field of the posterior columns. In addition to this is represented the manner in which the collaterals are given off and the termination of the central short tracts (which quickly bend again into the gray substance) of the anterior lateral columns, the "inland cells" (Golgi) in the posterior horn; the decussation in the posterior commissure is not clear. There are contained in the posterior roots apparently other individual fibres which have their neurone cells in the anterior horn, but in man this is not yet satisfactorily established. (Whitaker.)

receives the impulse and transmits it along the efferent neuraxone to neighboring motor neurones (and to the brain); (IV) the motor neurones respond to this stimulus by causing in certain muscles of the arm the contraction necessary to remove the hand from the painful object.

b. Voluntary Action.

In the mean time the sensory impulse has been transmitted to the brain and the individual becomes conscious not only that his hand has suffered an injury, but that a reflex act has occurred through which the hand has been removed from the immediate danger. The consciousness of injury aroused in the brain may be the stimulus to further acts on the parts of the organism toward further protection or toward repair of injury already done. These secondary and conscious acts of adaptation cannot be classified as reflex; they are voluntary acts, suggested by the brain, which in turn is actuated by the stimulus described above, possibly also by visual and other supplementary stimuli.

c. Nerve Centres.

1. **Centres in the Spinal Cord.**—In describing reflex action each segment of the cord has been described as a centre toward which afferent impulses come, and from which efferent responsive impulses are sent out. Each segment of the spinal cord is thus a *motor centre* for a limited number of muscles. But there are other centres in the spinal cord. There are centres which preside over: (I) the nutrition of tissues—*i. e., trophic centres* to muscles, nerves, bones, joints; (II) walls of bloodvessels—*i. e., vasomotors;* (III) secretion of skin—sweat centres; (IV) centres connected with *micturition, erection of the penis, parturition,* and *defecation.*

The motor, trophic, and vasomotor centres are distributed along the whole extent of the spinal cord; but the centres enumerated under (IV) are probably located in the lumbar enlargement of the cord.

2. **Centres in the Medulla Oblongata.**—In the spinal bulb, or medulla oblongata, there are numerous reflex centres, whose action will be discussed later:

(I) *Respiratory;* (II) *vasomotor;* (III) *cardiac centres;* (IV) also centres for *coughing, sneezing, mastication, deglutition, vomiting, co-ordinating, convulsor, closure of eyes, dilatation of pupil, salivary, sudorific, diabetic,* etc. Most of these centres are located in the floor of the fourth ventricle.

3. **Centres in the Brain.**—(*a*) **The Cerebellum** contains the following centres: (I) centres for the *co-ordination* of *movements;* (II) *emotional centres;* (III) *centres for muscle tonus.*

(*b*) **The Cerebrum** contains the following centres: (I) smell; (II) taste; (III) hearing; (IV) vision; (V) speech; (VI) various motor centres; (VII) thermogenic centres.

3. THE SYMPATHETIC NERVOUS SYSTEM.

The sympathetic nervous system is so called because it brings into harmonious and sympathetic action the work of the organs of the pleuroperitoneal cavity. This so-called system is not independent in action or separate in structure from the central nervous system.

a. Structure of the Sympathetic System.

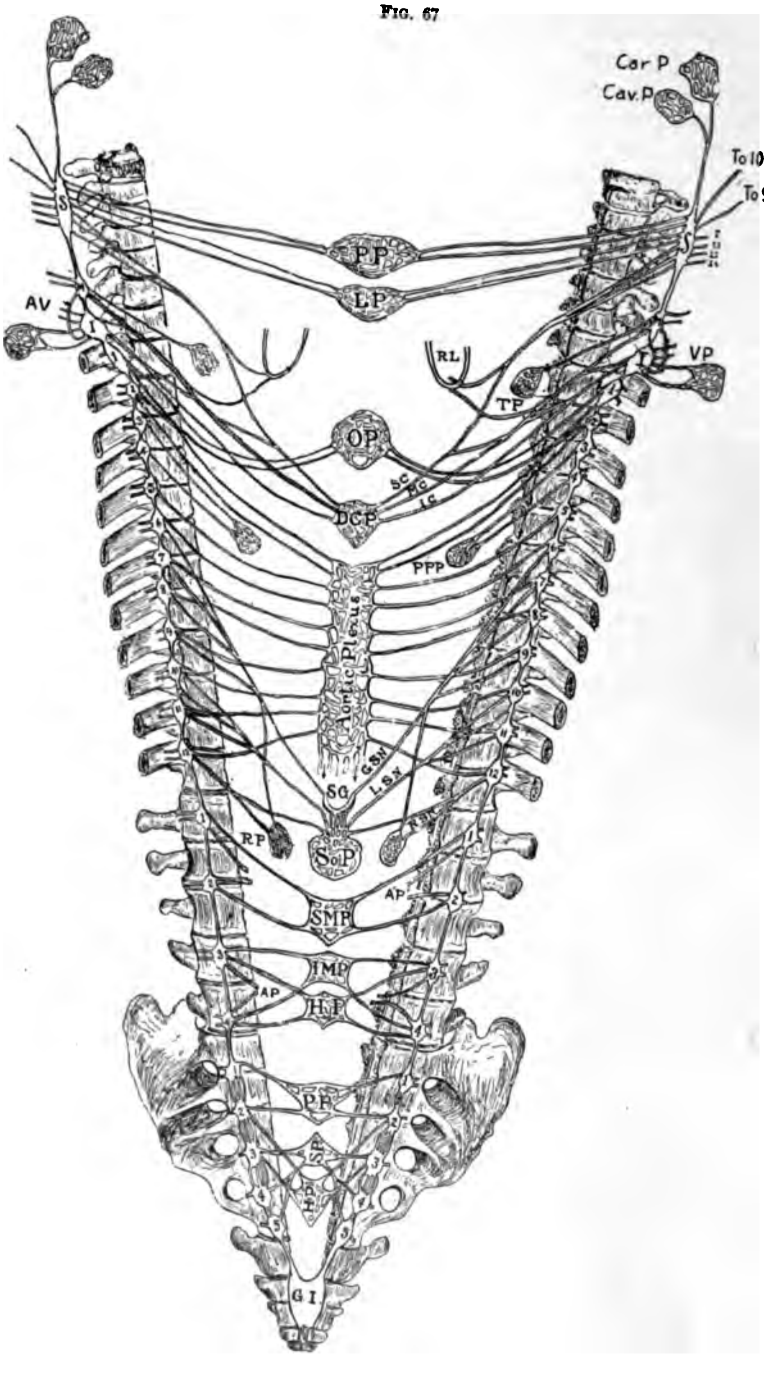
The sympathetic nervous system consists of a double chain of ganglia, one chain on each side of the vertebral column throughout the length of the vertebral column; the several ganglia of each chain corresponding roughly to the vertebral segments.

1. **The Cervical Sympathetic Chain.**—This chain of ganglia consists of three pairs called the superior, middle, and inferior cervical ganglia of the sympathetic system. The superior cervical ganglion receives communicating rami from the glossopharyngeal vagus and hypoglossal and the first four cervical nerves, and sends branches to the laryngeal plexus, to the external carotid plexus, to the cardiac plexus, and a communicating branch to the middle cervical ganglion. The middle cervical ganglion, besides having communication anteriorly with the superior cervical and posteriorly with the inferior, receives communicating rami from the fifth and sixth cervical nerves and sends branches to the thyroid gland and one branch to the cardiac plexus. The inferior cervical is joined to the first dorsal and the middle cervical, receives communicating rami from the seventh and eighth cervical, and sends a branch to the cardiac plexus.

2. **The Thoracic Sympathetic Chain.**—This consists of twelve ganglia joined with each other by communicating branches joined anteriorly with the inferior sympathetic directly and with the same ganglia indirectly through a trunk which passes ventral to the subclavian artery, thus completing a loop called the annulus of Vieussens. Each ganglion receives communicating rami from the corresponding intercostal nerves. The first five thoracic ganglia send branches to the aorta; the remaining thoracic ganglia contribute fasciculi to splanchnic nerves, which nerves in turn send branches to the œsophagus, to the aortic plexus, to the solar plexus, and to the suprarenal plexus.

3. **The Lumbar Sympathetic Chain** consists of five ganglia communicating with each other and with the corresponding lumbar

FIG. 67


Car P
Cav. P
To 10th
To 9th
S
PP
LP
AV
I
RL
VP
TP
OP
SC
MC
LC
DCP
PPP
Aortic Plexus
GSN
LSN
SG
RP
SoP
AP
SMP
IMP
AP
HP
PP
SP
HP
GI

erves in a manner somewhat similar to that described above for e other sympathetic ganglia. Each ganglion contributes branches the sympathetic plexuses of the abdominal and pelvic viscera.

4. **The Sacral Sympathetic Chain** is composed of five ganglia ith communications similar to those described for the preceding ortion of the sympathetic system and give contributions to the rge visceral plexuses of the pelvis, particularly to those of the lower owel and sexual apparatus.

5. **The Coccygeal Sympathetic Chain** consists of one ganglion ing ventral to the coccyx, and unpaired.

b. Visceral Plexuses of the Sympathetic System.

No attempt will here be made to describe in detail the numerous ources of these plexuses, though they have been mentioned individually above, or to describe the location of these plexuses. They ay be briefly listed as follows:

1. **Cervical Plexuses** of the sympathetic system: laryngeal, xternal carotid, and thyroid.

2. **Thoracic Plexuses:** cardiac plexus, superficial and deep, pulonary plexuses, anterior and posterior coronary plexuses, right and ft œsophageal plexuses, and aortic plexus.

3. **Abdominal Plexuses:** solar, suprarenal, and renal plexuses, and rterial plexuses, named after the several arteries which they accomany.

4. **Pelvic Plexuses:** hypogastric, rectal, uterine or prostatic, esicular, ovarian or spermatic, hemorrhoidal.

c. Function of the Sympathetic System.

The importance of this portion of the general nervous system in he control of the vital functions of the body can hardly be overstimated. It joins with the pneumogastric in the control of the eart and the digestive glands; it controls the blood supply to the arious tissues of the body; it controls the movements of the alimentary anal; it controls the activity of the kidneys and modifies the activity

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DESCRIPTION OF FIG. 67.

The sympathetic nervous system. Vertebral column split apart to make room for plexuses. , *M.*, and *I.*, superior, middle, and inferior cervical ganglia; 1 to 12, thoracic ganglia; 1 to 4, mbar ganglia; 1 to 5, sacral ganglia; *G. I.*, ganglion impar or coccygeal ganglion (enlarged); to *IV*, etc., branches of sympathetic to *I, II, III, IV*, spinal nerves, etc.; *Car. P.*, carotid lexus; *Cav. P.*, cavernous plexus; *P. P.*, pharyngeal plexus; *L. P.*, laryngeal plexus; *O. P*, sophageal plexus; *D. C. P.*, deep cardiac plexus; *P. P. P.*, posterior pulmonary plexus; *S. G.*, milunar ganglion; *G. S. N.*, *L. S. N.*, and *R. S. N.*, great, lesser, and renal splanchnic nerves; . *P.*, renal plexus; *S. M. P.* and *I. M. P.*, superior and inferior mesenteric plexus; *Hy. P*, ypogastric plexus; *A. P.* and *A′. P′.*, to aortic plexus; *P. P.*, pelvic plexus; *S. P.*, sacral plexus; . *P.*, hemorrhoidal plexus; *A. V.*, annulus of Vieussens. Aortic plexus shows upper and iddle section only.

of the organs of reproduction. The action of all these organs and system of organs is co-ordinated through the influence of the sympathetic system. The more important functions may be enumerated:

(*a*) *Cardioacceleration* and *cardioaugmentation* through the branches from the cervical ganglia.

(*b*) *Secretory impulses to the salivary glands,* the *stomach,* the *pancreas,* the *liver,* the *small intestine,* the *large intestine,* the *kidneys.*

(*c*) *Vasomotor impulses,* both *constrictor* and *dilator,* to all *arteries* and *arterioles.*

(*d*) *Motor impulses* to the muscular coats of the *stomach* and *intestines,* causing *peristalsis* and controlling the *pylorus* and the *cardia* of the *stomach.*

(*e*) *Motor impulses* to the muscularis mucosa of the alimentary canal, causing movements of the mucosa.

PART II.

SPECIAL PHYSIOLOGY.

Division A. NUTRITION.
THE PHYSIOLOGY OF THE INTERNAL RELATIONS.

Division B. MOTOSENSORY ACTIVITIES.
THE PHYSIOLOGY OF THE EXTERNAL RELATIONS.

Division C. REPRODUCTION.

DIVISION *A.*

NUTRITION.

Chapter III. CIRCULATION.
Chapter IV. RESPIRATION
Chapter V. DIGESTION.
Chapter VI. ABSORPTION
Chapter VII. METABOLISM.
Chapter VIII. EXCRETION

NUTRITION.

THE general term *Nutrition* is applied in Physiology to all of se activities, collectively taken, which are involved in supplying cells of the body with food, in building this food up into cell stance, in liberating the energy from it by katabolic processes d in ridding the body of the waste material, which results from se processes.

A general idea of the activities and organs involved in nutrition may be gained from the following table:

ACTIVITIES.		ORGANS OR TISSUES.
1. Perception.		Organs of the Special Senses.
2. *Prehension.*		Hands, Teeth, etc.
3. Preparation.		Hands, etc.
4. *Mastication.*		Teeth.
5. Deglutition.		Invol. Muscles of Pharynx and Œsophagus.
6. DIGESTION.		Secretory Apparatus: Gastric Glands, Liver, Pancreas, Intestinal Glands.
7. ABSORPTION.		Epithelium of Alimentary Canal.
8. CIRCULATION.		Blood and Lymph Circulatory Systems.
9. Selection.		Individual Cells of the body.
10. METABOLISM.	I. ANABOLISM.	Individual Cells of the body.
	II. KATABOLISM.	Individual Cells of the body.
11. RESPIRATION.	I. *External* R. [*Circulation* (b).]	Lungs, Air Passages, Muscles of Respiration.
	II. INTERNAL R.	Individual Cells of the body.
12. Rejection of waste products from the Cells of the body. [*Circulation* (c).]		
13. EXCRETION.	I. RENAL	Kidneys.
	II. *Pulmonary* . .	Lungs.
	III. *Cutaneous* . .	Sweat glands.
	IV. *Hepatic* . .	Liver.
14. *Egestion.*	1. *Micturition* . .	Bladder, etc.
	2. *Expiration* . .	Air passages.
	3. *Perspiration* . .	Skin.
	4. *Defecation* . .	Rectum.

To illustrate the table we may follow the steps of a cat's nutrition: (I) Through the organs of scent and sight she perceives her prey. (II) With claws and teeth the *prehension*, or catching, is accomplished. (III) The *preparation* is in this case a simple killing, but man prepares his food usually by cooking. (IV) She *masticates* it; (V) *swallows* it; (VI) *digests* it. (VII) The digested portion is *absorbed;* passes through the *circulation* (VIII) to the cells of the body, where each cell *selects* (IX) an appropriate part, which it *builds up* (anabolism) (X′) into cell substance. After a time the cell protoplasm is broken down (katabolism) (X″) incident to the functional activity of the cell; the balance of chemical affinity is immediately restored by the introduction into the cell of the oxygen (XI″) which has been brought from the *lungs* (respiration) (XI′) by the *circulatory* system. The products of katabolism are promptly *rejected* (XII) from the cell, carried to the periphery by the circulation, where they are *excreted* (XIII) by the proper organs and finally *ejected* (XIV) from the body.

After a moment's reflection it will be seen that—either directly or indirectly—*every organ* and *every function* of the *organism are brought into action in nutrition, except those of reproduction.*

Inasmuch as the circulatory system is variously and repeatedly involved in nutrition it will be more advantageous to treat that first than to interrupt the course of the discussion after the subject of digestion is opened. Respiration being a collateral branch of nutrition, a similar course may profitably be pursued regarding it. With an understanding of the circulation and respiration at command we may enter upon the uninterrupted discussion of digestion, absorption, metabolism, and excretion.

CHAPTER III.

CIRCULATION: INTRODUCTION.

A. THE COMPARATIVE PHYSIOLOGY OF THE CIRCULATION.

1. THE CIRCULATING FLUIDS.
2. THE ORGANS WHICH CAUSE THE CIRCULATION.

B. ANATOMIC INTRODUCTION.

1. THE BLOOD-VASCULAR SYSTEM.
2. THE LYMPHATIC SYSTEM
3. THE SPLEEN.
4. HISTOGENESIS OF THE CIRCULATORY ORGANS AND TISSUES

C. PHYSICAL INTRODUCTION.

1. THE FLOW OF LIQUIDS THROUGH TUBES.
2. MANOMETERS.

THE PHYSIOLOGY OF CIRCULATION.

A. CLASSIFICATION OF THE FLUIDS, TISSUES, AND ORGANS.

B. THE CIRCULATING FLUIDS.

1. THE BLOOD.
    - I. THE PHYSICAL PROPERTIES.
    - II. THE MORPHOLOGY OF THE BLOOD.
        - *a*. The Red Blood Corpuscles.
        - *b*. The White Blood Corpuscles.
        - *c*. Other Structural Elements of the Blood.
        - *d*. Plasma.
    - III. THE CHEMICAL PROPERTIES OF THE BLOOD.
    - IV. THE FUNCTIONS OF VARIOUS PARTS OF THE BLOOD
    - V. THE TOTAL QUANTITY OF THE BLOOD.
    - VI. THE PROTECTION OF THE BLOOD SUPPLY.
        - 1. The Location of the Vessels.
        - 2. The Influence of the Intima.
        - 3. The Coagulation of the Blood.
    - VII THE EFFECT OF HEMORRHAGE.
    - VIII. THE TRANSFUSION OF BLOOD
2. THE LYMPH.
    - I. THE PHYSICAL PROPERTIES.
    - II. THE MORPHOLOGY OF THE LYMPH.
    - III. THE CHEMICAL PROPERTIES OF THE LYMPH.

C. THE FORMATION AND DESTRUCTION OF THE CORPUSCLES.

1. THE ORIGIN OF THE RED BLOOD CORPUSCLES.
2 THE DECAY OF THE RED BLOOD CORPUSCLES.
3. THE FORMATION AND DESTRUCTION OF LEUKOCYTES.
4. SUMMARY OF THE FUNCTIONS OF THE SPLEEN.

D. THE CIRCULATION OF THE FLUIDS.

1. THE ACTION OF THE HEART.
2. THE CIRCULATION OF THE BLOOD.
    a. The Circulation in the Arteries.
    b. The Circulation in the Capillaries.
    c. The Circulation in the Veins.
    d. The Coronary Circulation.
3. THE CIRCULATION OF THE LYMPH.
    a. In the Lymph Radicals.
    b. In the Lymphatics.

E. THE CONTROL OF THE ORGANS OF CIRCULATION.

1. THE INNERVATION OF THE CIRCULATORY SYSTEM.
    a. The Innervation of the Heart.
    b. The Innervation of the Arteries.
2. ADAPTATIVE CO-ORDINATION OF THE ACTIVITIES OF THE CIRCULATORY ORGANS.

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THE PATHOLOGIC PHYSIOLOGY OF THE BLOOD.

INTRODUCTION.

A. CORPUSCLES.

1. THE RED CORPUSCLES.
    a. Morphology.
        (1) *Form Modified.*
        (2) *Size Modified.*
    b. Color.
        (1) *Hæmoglobin Increased*
        (2) *Hæmoglobin Decreased.*
    c. Number.
        (1) *Increased.*
        (2) *Decreased.*
2. THE WHITE CORPUSCLES: LEUKOCYTES.
        (1) Increased.
            a. Simple Leukocytosis.
            b. Mononuclear Leukocytosis.
            c. Polynuclear Leukocytosis, or Neutrophilia.
            d. Eosinophilia.
            e. Myelæmia.
        (2) Decreased.

B. PLASMA.

ATER.

ALTS.

- (1) The Chlorides
- (2) The Phosphates.
- (3) The Sulphates.
- (4) Calcium Salts.

EXTRACTIVES.

- (1) Dextrose.
- (2) Urea.
- (3) The Purin Bodies.

C. COAGULATION FACTORS.

- (1) Fibrinogen.
- (2) Thrombin.
- (3) Calcium Salts.

E PATHOLOGIC PHYSIOLOGY OF THE CIRCULATORY ORGANS.

INTRODUCTION.

1. PERICARDITIS.
   - *a.* Acute.
   - *b.* Chronic.
2. MYOCARDITIS.
   - *a.* Acute.
   - *b.* Chronic.
3. ENDOCARDITIS (ACUTE).
   - *a.* Thrombosis.
   - *b.* Embolus.
4. ENDOCARDITIS (CHRONIC). VALVULAR DISEASES.
   - *a.* Aortic Disease.
     - *I. Insufficiency.*
     - *II. Stenosis.*
   - *b.* Mitral Disease.
     - *I. Insufficiency.*
     - *II. Stenosis.*
   - *c.* Disease of Pulmonary Valves.
   - *d.* Tricuspid Insufficiency.
5. DILATATION AND HYPERTROPHY.
6. ARTERITIS.
   - *a.* Acute.
   - *b.* Chronic.
7. ANEURYSM.
8. PHLEBITIS.
   - *a.* Acute.
   - *b.* Chronic.

INTRODUCTION.

As soon as an animal attains to the dignity of an individual of the third order (see Individualization of Living Substance, Gen. Physiol., Part I.)—*i. e.*, as soon as it has more than an ectoderm and endoderm—the necessity arises of conveying to the middle layer or mesoblast the nourishment obtained from the environment by the layers which lie in immediate contact with the environment. And thus the circulatory system is born of necessity. It is a system of tubes taking up fluid food and oxygen from the hypoblast and conveying it to all parts of the body. This system of tubes, filled with a fluid kept in circulation through the agency of the heart, has fine ramifications in all parts of the body, and serves not alone to carry nourishment, but also to remove the waste material from the active cells. Further, the blood serves as a distributor of warmth and moisture in the body.

A. THE COMPARATIVE PHYSIOLOGY OF THE CIRCULATION.

The primary object of the circulation is the distribution of nutriment to tissues which do not lie in or adjacent to absorbing surfaces. Secondarily, the fluids in circulation carry oxygen from the absorbing surfaces to the other active tissues, and finally these fluids carry to the periphery of the organism for excretion certain waste products which are of no further use to the system. As a "common carrier" the circulatory system is the servant of the fundamental process of nutrition. In each one of its various capacities it seems to be essential to the organism.

In the description of this system it is convenient to treat (I) the circulating fluids, and (II) the organs which cause the circulation of the fluids.

1. THE CIRCULATING FLUIDS.

(*a*) **The Most Primitive Condition** is represented by the *cœlenterates*, whose *gastrovascular* system of canals is filled with a fluid which is composed of the digested or partly digested ingesta and of imbibed water. This fluid may be called a *circulating chyme*. It is devoid of corpuscular elements. The oxygen which it holds in solution may be absorbed by the cells which are adjacent to the canals, but it lacks any special agent to serve as an oxygen carrier.

(*b*) **Next in Order** as a circulating fluid may be considered the *circulating chyle* or *hydrolymph* of *echinoderms*, *lamellibranchiate molluscs*, *tunicates*, and the *amphioxus*. This fluid differs from the circulating chyme in having passed into the organism through an absorbent surface of epithelium. It is a selected fluid and, therefore, much more uniform in its composition than is the crude circulating chyme. This circulating chyle is corpusculated. The corpuscles are not particularly abundant and are similar to the lymph corpuscles and leukocytes of higher vertebrates—being capable of amœboid movements and varying much in size.

(*c*) **The Term** *hæmolymph* is applied to the circulating fluid possessed by *worms*, most *molluscs*, and *arthropods*. Hæmolymph is distinguished from hydrolymph in having *hæmoglobin* or other oxygen carrier *in solution*.

(*d*) **The Most Complete System** of circulating fluids is possessed by the vertebrates (amphioxus excepted). The circulating chyle is received into the lymphatic system of vessels and mixed with true lymph. This soon mixes with the blood—the most complex of all circulating fluids. The blood of vertebrates consists of (1) a fluid plasma, quite like the fluid portion or plasma of the lymph, (2) corpuscular elements which in turn are: (I) the leukocytes, which are practically the same as the lymph corpuscles; (II) the red corpuscles, which are characteristic of the vertebrates, though they have been also observed in a few isolated invertebrate genera. The essential feature of the red blood corpuscle is *hæmoglobin*.

The hæmolymph contains various oxygen carriers, or respiratory pigments (hæmoglobin, hæmerythrin, hæmocyanin), in solution, while *the blood contains hæmoglobin in corpuscular form*. These hæmoglobin corpuscles are retained within a definite system of canals, the *blood-vascular* system; while the lymph circulates in a vasolacunar system similar to that possessed by most of the invertebrates. Note: (I) that in the *circulating chyme* the sole function of the fluid is to carry nutriment; (II) that the hydrolymph carries nutriment to the tissues and excrement from them; (III) that the hæmolymph carries *nutriment and oxygen* to the tissues and excrement from them; (IV) that in the blood-lymph systems the same functions are performed, but there is a differentiation of structure and composition between blood and lymph and the functions are performed more perfectly because of this specialization.

2. THE ORGANS WHICH CAUSE THE CIRCULATION.

(*a*) **The Cœlenterates** have a system of canals which are really diverticula from the gastric cavity. The fluid within this *gastro-vascular* system of *canals* is set in motion by the general movements of the animal.

(*b*) **The Lowest Order** of circulatory system is that in which the hydrolymph and hæmolymph of the invertebrates flow. As a general rule the lymph is kept in motion by the rhythmical contractions of some portion or portions of the canal system. These pumping organs are called *hearts*. The animal kingdom presents hearts of various forms and degrees of complexity, but they all have this in common that they represent dilatations of the blood-vessels. In mollusca and arthropoda the heart is located dorsally, in vertebrates it is ventral. There are two general methods of propulsion: (I) *Peristalsis*. The earthworm possesses a series of segmental arterial arches connecting the ventral and dorsal trunks. The rhythmic peristalsis of these arches keeps the blood (hæmolymph) in circulation. The amphioxus has a similar system physiologically; the contractile portions are upon the ventral vein, forcing the lymph to the branchial system (respiratory heart) and upon the dorsal artery, forcing the lymph through the systemic capillaries (systemic heart). (II) *Pumping*. The second method of propulsion is by a force-pumping mechanism, the essential features of which are the strong muscular walls, the valves, and the filling chambers. The first of these ensures a comparatively quick and strong contraction of the walls of the heart upon the fluid contents, but the pressure (intraventricular) is equally distributed over the walls of the organ and the fluid is as likely to go back through the way by which it entered as to go forward unless it be blocked. The valves at the entrance of the heart stop this regurgitation and ensure the forward movement of the circulating fluid. To be mechanically effective the heart must fill quickly. This necessity is satisfied in arthropoda by a filling chamber around the heart—the pericardium—into which the blood flows during cardiac contraction. When the heart relaxes the collected lymph quickly enters its cavity through the open valves. A similar function is performed by auricles in the mollusks.

In most invertebrates the blood escapes into tissue spaces at the end of its arterial flow.

After traversing the tissue spaces and LACUNÆ the lymph makes its way into the vessels, which return it to the organ of propulsion. The lacunæ and tissue spaces of invertebrates correspond to the lymph or serous cavities and lymph radicles of the higher animals.

(*c*) **The Vertebrates**—above amphioxus—possess the highest type of circulatory system—the blood is propelled by a heart fully equipped with valves and filling chambers. The amphioxus has two hearts—respiratory and systemic. Fishes have a respiratory heart whose strength is sufficient to carry the blood through the systemic vessels after it has been aërated.

In the amphibia and lower reptiles there are two auricles, but only one ventricle, which must serve both as respiratory and systemic heart. In these animals there is, to a certain extent, a mixture of the aërated and unaërated blood. The devices for ensuring the purer blood current for the cephalic end of the animal are, to say the least, ingenious. In crocodiles, birds, and mammals the heart is double, each half being composed of an auricle and a ventricle. The right half of the heart is the respiratory heart and the left side the systemic heart.

The morphologic details by which these various points are accomplished are matter for anatomy rather than for physiology.

B. ANATOMICAL INTRODUCTION.

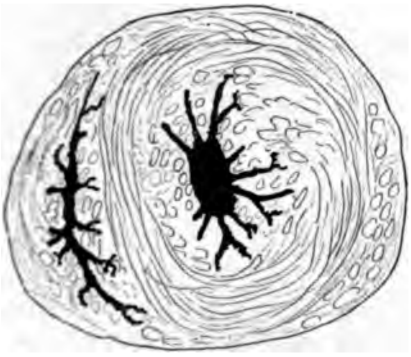
1. THE BLOOD-VASCULAR SYSTEM.

Structural features of the heart and vessels which are of especial physiologic importance.

a. The Heart.

1. **The Musculature.**—(*α*) Several muscle layers—longitudinal, oblique, and circular—so intricately arranged that one system of fibres may often be traced in all of the directions in turn.

FIG. 68



Cross-section through a completely contracted human heart, at the junction of the middle and lower thirds. (Krehl.)

FIG. 69

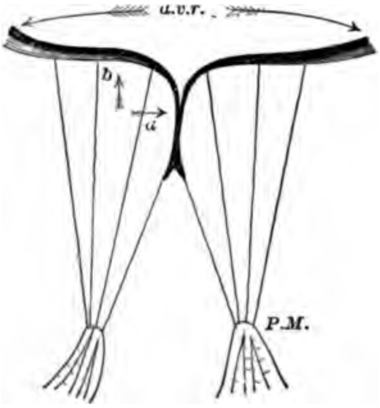


Diagram showing the general arrangement of the auriculoventricular valves: *a.v.r.*, auriculoventricular ring; *a*, plane of tangency; *P.M.*, papillary muscles. (After Krehl.)

(*β*) Many fibres or bundles arise from the auriculoventricular ring, and after making their circuit, return again to an opposite segment of the ring.

(*γ*) Some bundles arise from the ring, make their winding circuit, and terminate in a papillary muscle.

(δ) The bases of the aorta and pulmonary arteries are surrounded by circular heart fibres, and, further, many of the longitudinal fibres arise from the region of the great vessels.

(ε) The musculature of the left ventricle is very much heavier than that of the right (Fig. 68).

2. **The Valves.**—(α) From the auriculoventricular ring valves, convex on the auricular surface, project toward the centre of the ring.

(β) Each cusp, or flap, is much thicker near its origin on the ring than near the free margin.

(γ) Each cusp is stayed or guyed, from the ventricular side, by several tendinous cords which pass from the apex of a papillary muscle to different parts of the cusp (Fig. 69).

(δ) The cusps meet at *a*, not in a common tangent line, but in a common tangent plane.

3. **The Cavity of the Heart.**—(α) The dilated cavity of the left ventricle is an inverted oblique, quadrilateral pyramid, presenting irregularities of surface, due to columneæ carneæ and papillary muscles. Its volume in the adult male is about 180 c.c.

(β) The contracted cavity of the left ventricle presents in the upper segment a quadrilateral outline, in the lower segment a triangular outline. From the central cavity, which at the end of systole may be almost obliterated, numerous crevasses pass out into the wall of the ventricle. These crevasses represent spaces between the fleshy columns or papillary muscles (Fig. 68).

(γ) The dilated cavity of the right ventricle presents, on cross-section, a crescentic outline. It is much shorter than the cavity of the left ventricle, though its volume is the same.

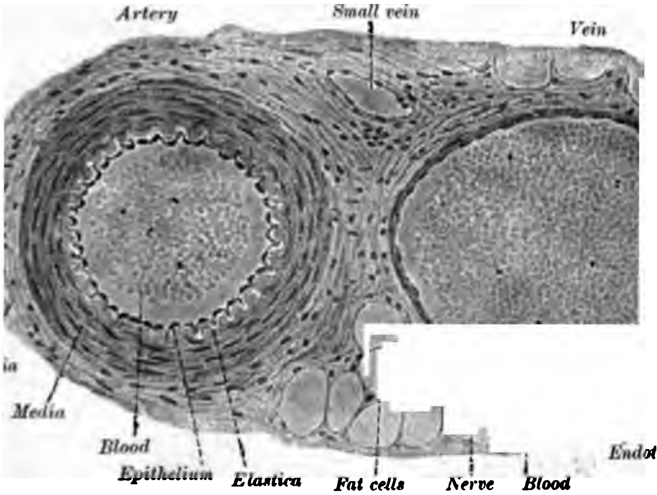
(δ) The closed cavity of the right ventricle presents a series of irregular crevasses which together describe a crescentic field (Fig. 68).

b. The Bloodvessels.

1. **The Arteries and Veins** are composed of practically the same elements in the same arrangement; the principal difference being the proportion of the different tissues entering into the composition of the several layers. The walls of the arteries are thicker, very much thicker (Fig. 70).

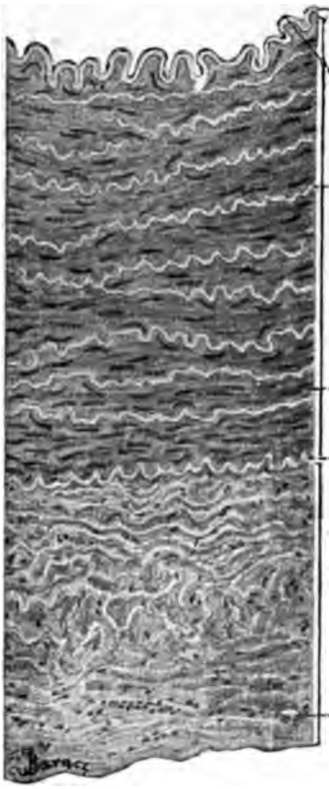
This is important for the following considerations: First, the greater thickness enables them to sustain the greater blood pressure. Second, their greater resistance enables them to withstand minor external pressure—*e. g.*, from muscular contraction or pressure of clothing; thus the parts supplied are subjected to a minimum accidental variation of blood supply. Third, their greater thickness makes them less vulnerable in accidents. The large arteries have

FIG. 70



nsverse section through a microscopic artery and vein in epiglottis of a child. (Szymonowicz.)

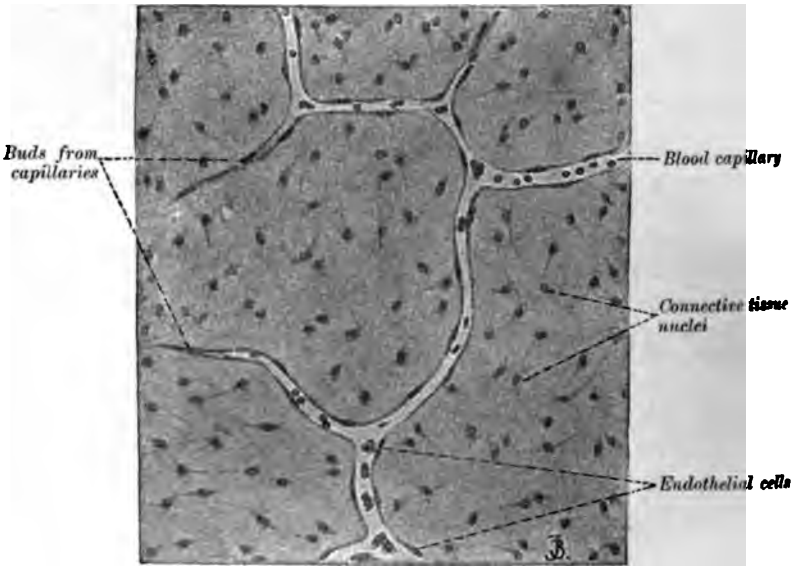
FIG. 71



Section of thoracic aorta. (Szymonowicz.)

relatively more elastic tissue, while the small arteries and arterioles have relatively more muscle tissue. The reason is evident: The large vessels receive the direct impulse from the heart beat. The heart can rest a part of the time. The walls of the arteries are under continuous, though varying strain. Muscle tissue alone could not long endure the strain of unremitting work; only the unsensitive, unresponsive, elastic tissue can be safely put to so prodigious a strain. In the small arteries and arterioles the lateral pressure is very much less. The muscle fibres of these vessels, supplemented by a small amount of elastic tissue, are quite sufficient to sustain it. Further, the supply of blood to special organs is controlled by these muscle fibres acting under the influence of the vasomotor nerves.

FIG. 72



Formation of capillaries in embryonic tissue. (Szymonowicz.)

2. **The Capillaries.**—The capillary wall, consisting as it does of simple endothelial plates, cannot withstand much pressure. Most of the energy exerted by the heart has been expended in overcoming the resistance between the heart and the capillaries, so that the millions of capillaries are easily able to withstand the distributed remnant of pressure. Any increase of capillary pressure tends to increase the spaces between the endothelial plates, and thus in turn to facilitate not only diapedesis of white blood corpuscles, but transudation of plasma.

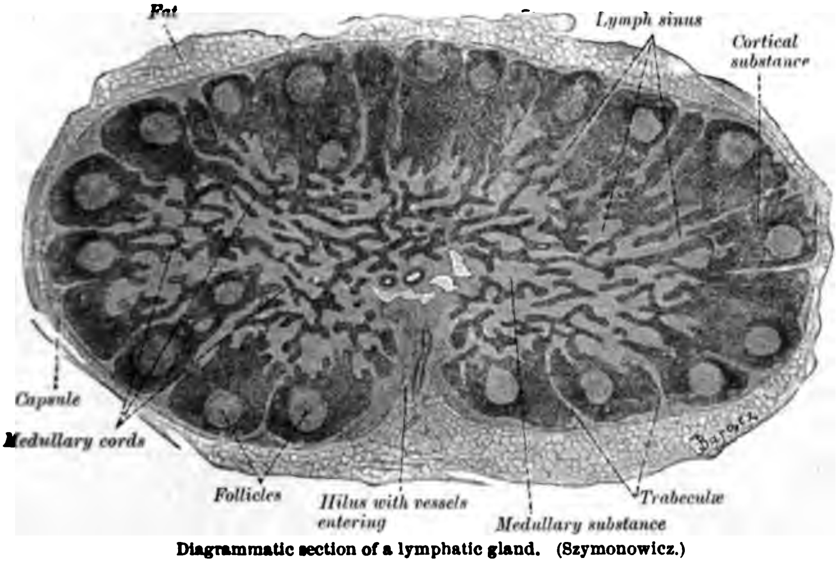
2. THE LYMPHATIC SYSTEM.

a. Lymphatic Follicles and Glands.

Lymphatic tissue is composed of two elements: 1st. A connective-tissue reticulum associated with stellate connective-tissue cells. This is called the *Adenoid Reticulum.* 2d. Small round cells which are enclosed within the meshes of the reticulum (Fig. 71). The lymphatic tissue, or adenoid tissue, is frequently found in small quantities along the arteries associated with the perivascular lymph channels, but it is usually collected in well-defined structures called lymph follicles.

1. **Lymph Follicles** are simple lymphatic nodules, which occur in great numbers in the mucous membrane of the respiratory and alimentary tracts. Each follicle is surrounded by a delicate but close-meshed wall or capsule of fibrous connective tissue. Within this capsule the whole space is filled with typical lymphatic and adenoid tissue.

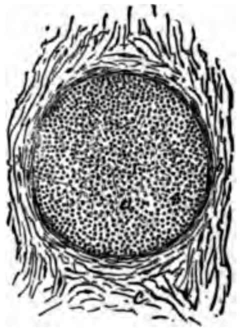
FIG. 73



Diagrammatic section of a lymphatic gland. (Szymonowicz.)

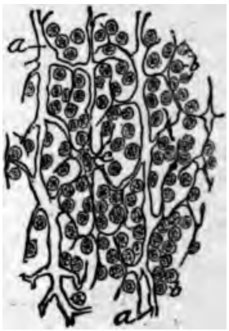
A lymph follicle receives its blood supply from a vascular envelope composed of a loose meshwork of arterioles, from which capillary loops penetrate to the centre of the follicles and return the venous blood to the corresponding meshwork of venules. Each follicle has an *afferent lymphatic,* which brings a stream of lymph which oozes through the adenoid tissue, and, emerging with fewer old leukocytes and more young ones, is carried off by the *efferent lymphatic.* Within the follicle old leukocytes, which come laden with different materials gathered in their wanderings, become helplessly entangled in the adenoid meshes and disintegrate. Within the follicle is a closely packed group of leukocytes, which are undergoing rapid reproduction by karyokinesis. Such a group of leukocytes is called a *Lymph Knot*, and this is the source of the young leukocytes which join the efferent stream. So the efferent stream from a lymph follicle or lymph gland may not contain more leukocytes than the afferent stream, but there will be more young active ones and fewer old sluggish ones (Fig. 74).

FIG. 74



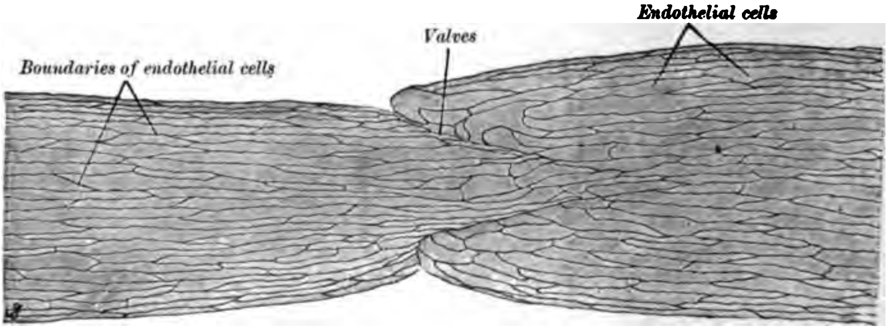
Simple lymph follicle from conjunctiva of a dog: *a*, lymphoid tissue, limited by the fibrous capsule (*b*); *c*, surrounding connective tissue. (After Piersol.)

FIG. 75



Elements of adenoid tissue from partially brushed section of lymphatic gland of a child: *a*, fibres of reticulum; *b*, lymphoid cells; *c*, expanded connective-tissue plate. (After Piersol.)

FIG. 76



A lymph vessel. (Szymonowicz.)

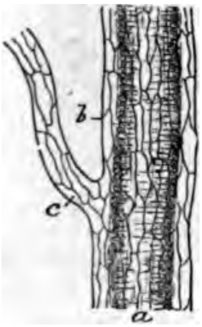
2. **A Lymph Gland** is simply a collection of lymph follicles. The structural variations are shown in Fig. 73. The functions are the same. The favorite locations of the lymphatic glands seem to be the *mesentery*, the groin, the axilla, and the neck; though they are very generally but sparsely distributed in subcutaneous tissues.

b. Lymphatics or Lymph Vessels.

1. **Lymph Radicles and Lymph Capillaries.**—A lymph radicle or rootlet is simply a connective-tissue space which is lined with endothelial plates. These spaces are very irregular, sometimes narrow chinks and crevasses, sometimes comparatively wide spaces.

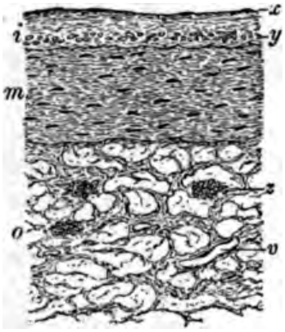
Lymph capillaries conduct the lymph from these irregular *collecting spaces* to the lymph vessels. Even the capillaries and the smaller lymphatics are irregular in lumen.

Fig. 77



Perivascular lymphatic (*b*) enclosing a small artery (*a*), from the silvered mesentery of frog; *c*, branching lymphatic capillary. (After Piersol.)

Fig. 78



Transverse section of human thoracic duct: *i*, *m*, and *o*, respectively, the inner, middle, and outer tunics; *x*, endothelial lining, beneath which lies the fibrous stratum containing network of longitudinal elastic fibres (*y*); *z*, longitudinally disposed bundles of muscular tissue within adventitia; *v*, capillary bloodvessels. (After Piersol.)

2. **Lymph Trunks.**—All of the larger lymph vessels are provided with valves. The larger trunks have a regular lumen and walls quite like those of a bloodvessel.

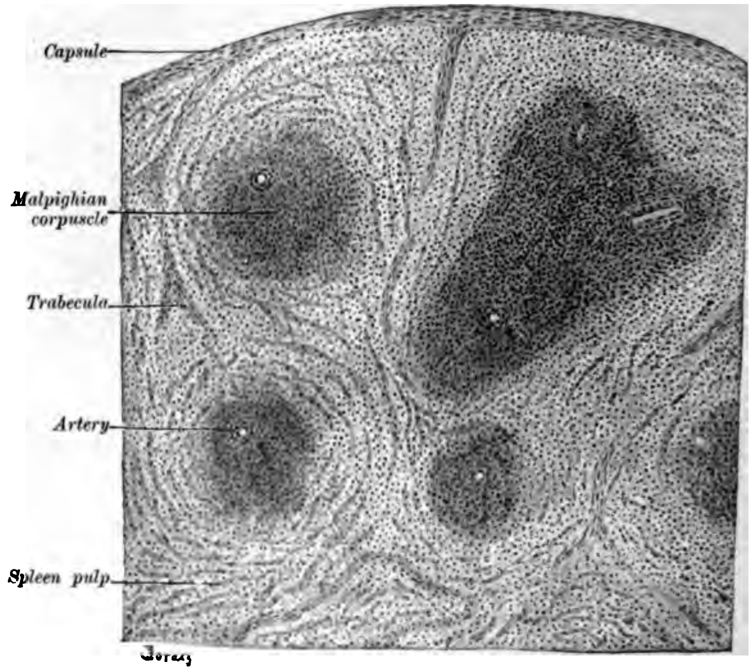
3. THE SPLEEN.

1. **Development.**—In the human embryo its development begins about the end of the second month. Its beginning may be found in the mesentery posterior to the stomach, and immediately dorsal to the duodenum. At this point a very small terminal branch of the cœliac artery, the future splenic artery, shows in the perivascular lymph channels an accumulation of large lymphoid cells with large granular nuclei. The steps of the development are: the progressive development of lymphatic tissue; the penetration of the mass by terminal branches of the advancing splenic artery; the development of non-striated muscle tissue around the arterial branches, and in a coarse meshwork throughout the mass; the pushing out of the mesen-

tery which forms a splanchnopleuric cover for the spleen, and the definite encapsulement of the organ with connective tissue and non-striated muscular tissue.

2. **Structure.**—Inasmuch as the spleen begins in a development of lymphatic tissue, it is to be expected that its structure is analogous to that of a lymph gland. Such is the case. The spleen sustains to the blood-vascular system somewhat the same relation that the lymph glands sustain to the lymph-vascular system, and the blood oozes through the spleen reticulum in much the same way that lymph oozes through a lymph gland.

FIG. 79



Section of spleen. (Szymonowicz.)

4. HISTOGENESIS OF THE CIRCULATORY ORGANS AND TISSUES.

The circulatory system is that system which more than any other is shut off from the outside world. One would expect that this system of organs, which is, *par excellence*, a system devoted to internal relations, should be derived from the entoderm; and it is. Remember that the *entoderm* is early differentiated into hypoblast, mesoblast, and notocord. In this differentiation the mesoblast has withdrawn farther from the outside world than was the entoderm. The mesoblast early divides into primitive segments—somatopleuric, and splanchnopleuric mesothelium and *mesenchyme*. The last named arises latest and is derived from the first three (Hertwig). From the mesenchyme are derived all the organs and tissues of the circulatory system: (I) The blood itself is purely a derivative of the mesenchyme. (II) The bloodvessels and lymphatics are also derived solely from the mesenchyme—viz., the endothelial layer of the intima, the involuntary muscle fibres of the media, and the elastic fibres of the vessel walls. (III) The spleen, lymphatic glands, and the red-marrow of bones are also wholly mesenchymal tissues. The nerves which supply the muscles of the heart and bloodvessels are derived from the ectoderm, and are distributed to the circulatory system through the vagosympathetic nervous system.

C. PHYSICAL INTRODUCTION.

1. THE FLOW OF LIQUIDS THROUGH THE TUBES.

The analogy between the nervous system and a telegraphic system is a striking one, and frequently cited; even more striking is the analogy between the circulatory system and the water-supply system of a city. The water supply starts from a central pumping station—or elevated reservoir—passes through large mains at first, and is distributed through branches that are smaller and smaller as they subdivide on their way to different houses. The blood supply starts from the centrally located, pumping heart, passes through large trunks at first, and is distributed through branches that get smaller and smaller as they subdivide on their way to different tissues.

The physical laws of the circulation are the physical laws of the flow of liquids through tubes. No adequate knowledge of the circulation can be had without first a knowledge of the physical laws.

a. The Flow of Liquids under Continuous Pressure.

"*The flow of liquid is caused by a difference of pressure between the different parts of a mass of liquid.*" (Daniell.)

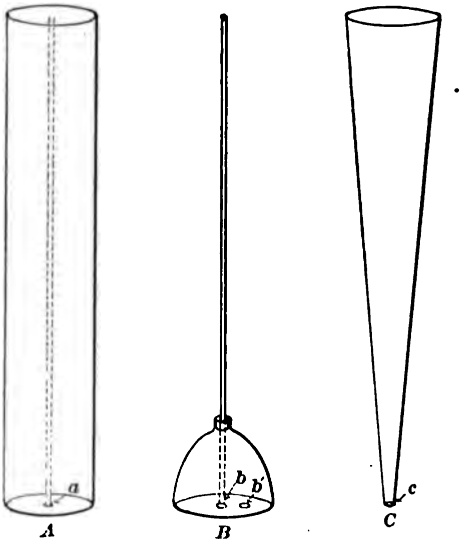
The attraction of the earth—gravitation—furnishes the continuous pressure which causes a flow of liquids along channels or through tubes. The conditions necessary are an elevated source and a low outlet. Let us take, for example, a reservoir as a source of flow. Let an aperture be made in the reservoir any distance (h) below the surface of the water. The pressure upon the water just inside the aperture is greater than pressure at the surface—atmospheric pressure

—because it supports the weight of the superposed water. It will, therefore, flow away from the higher pressure within the aperture toward the lower pressure without the aperture.

1. **Velocity.**—Torricelli's Law: *The rate at which a liquid is discharged through an orifice in the wall of a reservoir is equal to the velocity which would be acquired by a body falling freely through a height equal to the distance between the orifice and the surface of the liquid.*

From the law of falling bodies we know that *the velocity* (v) *is equal to the square root of twice the product of the height by the acceleration due to gravitation* (g)—*i.e.*, $v = \sqrt{2gh} = \sqrt{2 \times 981 \times h} = 44.3\sqrt{h}$. Velocity thus obtained is expressed in *centimetres per second.*

FIG. 80

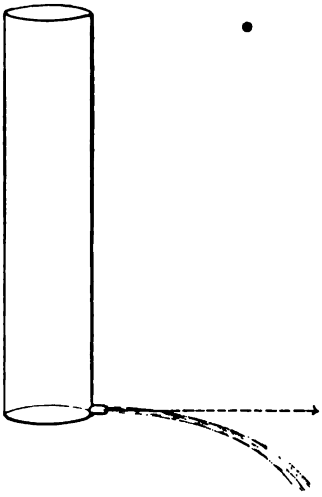


Reservoirs.

2. **Discharge.**—Within reasonable limits velocity is not modified by the size of the aperture. Discharge (D), on the other hand, is equal to the product of the area (a) of the jet by the velocity. One would think that the area of the jet would equal the area of the aperture, but such is not the case. The fluid streams toward the aperture from various directions, and the jet is, in a way, a resultant of the various streams just referred to, and *emerges convergent* to reach a minimum diameter in the "*vena contracta*" very near the aperture. The real diameter of the jet is the diameter of the *vena contracta*. A practical verification of the principle is much simplified by inserting into the aperture a short, smooth nozzle. The diameter of the jet will equal the diameter of the nozzle. The discharge (D)

:he product of the area of the jet (a) by the velocity (v)—*i. e.*, $\times$ v, but $a = \pi r^2$ and $v = 44.3\sqrt{h}$; therefore, $D = 44.3\pi r^2\sqrt{h}$. that 44.3π represents a constant factor in all experiments; so e discharge will vary as the square of the radius of the jet : square root of the height—*i. e.*, D varies as $r^2\sqrt{h}$.

FIG. 81



Reservoir with lateral nozzle.

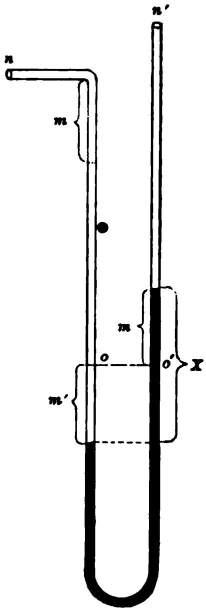
:essure.—The pressure may be looked upon as the stress ne liquid at the point of observation. Take, for example, ssure of the water on the bottom of a reservoir (Fig. 80). square centimetre of the bot- ipports the weight of the of water whose vertical di- 1 is the depth of the water, iose area (a) is 1 sq. cm. The the bottom of the reservoir is 'actor in the pressure. The f the water is the only matter ortance. In reservoirs B and ›ressure upon area (1 sq. cm.) s the same as that upon area a rvoir$A$, because the height of imn is the same.

reservoir B the pressure on is equal to that on area a, so e pressure on area b' equal that ı a or area b, because *the fluid insmit pressures equally in all ns.* Then the lateral pressure the bottom of the reservoir e as great as the downward e. In the reservoir shown in Fig. 80 the pressure at the would be found by finding the weight of a volume of liquid area equals the area of the lumen of the nozzle, and whose is the depth of the liquid above the middle of the lumen of zzle.

he Measurement of Pressure. (a) *The Unit.*—The pressure liquid or the stress of the liquid at the point of observation ce that may be expressed in units. To express this force in P (in dynes per 1 sq. cm.) $= hgs$, $h =$ depth of liquid, $g =$ ation of gravitation (981), $s =$ specific gravity. It is customary, r, to express the pressure in height above orifice or "head," ignore the factors g and s. This is especially convenient : the pressure is usually measured with a mercury manometer ›ressed in "centimetres of mercury," meaning that the pressure :ient to support a column of mercury so many centimetres

(β) *The Mercury Manometer.*—(See Fig. 82.) This instrument consists of a U-shaped tube, one of whose limbs is usually bent at right angles to facilitate its junction with other apparatus. Both ends of the tube (n and n') are left open. That limb through which the pressure is transmitted (n) is called the ***proximal limb***, the other the ***distal limb***. When the pressure is positive the mercury will rise in the distal limb; when negative it will fall in the distal limb. The rise in the distal limb (m) will be accompanied by a corresponding fall in the proximal limb (m'); the total pressure will be represented by a column of mercury equal to $2m$ or x. But a part of that pressure is due to an introduced error when the fluid in the proximal tube above the mercury is water or blood, or a salt solution. One introduces more of this (in centimetres) than was in the proximal tube before. If the fluid which has been introduced with the fall of the mercury in the proximal column is, say, $\frac{1}{13}$ the density of mercury, then if $m = 13$ cm., the real rise of mercury due to initial pressure is represented by 26 cm. of mercury minus 1 cm. of mercury correction, or 25 cm. mercury.

FIG. 82



Mercury manometer.

Let us express the relations in more definite terms. Suppose the proximal limb to be filled with water (sp. gr. Hg = 13.596). The corrected height (h) of the column of mercury, when m is the rise in the distal column:

$$h = 2m - \frac{m}{13.596} = \frac{27.192m - m}{13.596} = \frac{26.192m}{13.596}.$$

(I) *The pressure in grams per unit area* (p) is equal to the height of the column multiplied by the *sp. gr.* of mercury.

$$p = hs = \frac{26.192m}{13.596} \times 13.596 = 26.192m = ca.\ 26.2m.$$

One may readily get the pressure per square centimetre by ***measuring in centimetres the rise of mercury in the distal column and multiplying that by*** 26.192 (26.2).

(II) *The pressure in dynes per unit area* (P) is found by simply multiplying p by g, for $P = hgs$ and $p = hs$.

$$P = hgs = 981 \times 26.192m = 25694m \text{ dynes per square centimetre.}$$

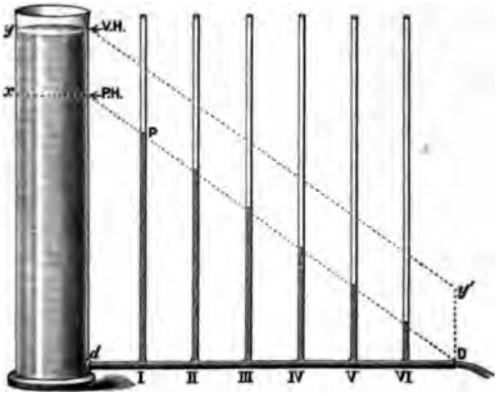
To express the pressure in dynes per square centimetre one has only to observe m ***and multiply that by*** 25694.

(γ) *The Piezometer* is a simple instrument consisting of an upright tube connected directly with the point at which the pressure e measured. (See Fig. 83, I, II, etc.) The pressure at the causes the liquid to rise in the piezometer until the weight column balances the pressure at the base. To compute the ynes or the p in grams one applies the principles given above mercury manometer: h equals the rise in the tube, as there orrection in this case. s for water would equal 1; so that and $P = 981h$.

ick's Spring Manometer, the Sphygmoscope, Tambours, Piston, and other instruments of the same class are for the ation of varying pressures, and are constructed rather for tive than for quantitative observations.

he Pressure of Liquid Flowing through Tubes.—Fig. 84 illusn experiment with a reservoir, a horizontal delivery tube, eries of piezometers. The piezometers indicate faithfully the

FIG. 83



Reservoir with piezometers.

e of the liquid at the point where they are severally in comtion with the delivery tube. The pressure in piezometer I r than that in II, that in II is higher than that in III, and so ote that the pressures are progressively and regularly less as ceed from the reservoir to the end of the delivery tube. If ere only one piezometer, and that located at position VI, the ould maintain the same level which it shows in the first experi- If there were sixty piezometers instead of six along the elivery tube, the water in every piezometer would rise to the D. This line is called the *pressure slope.*

is the pressure less in VI than in V? When the stream of as reached the point VI it has still to overcome the resistance n that point and the delivery (D). The pressure upward at st the same as the pressure to the right—*i. e.*, the weight of umn of liquid in piezometer VI just balances the "back pressure" or resistance to the flow to D. Piezometer V measures the resistance beyond V, and therefore must stand higher. The reservoir may be looked upon as a gigantic piezometer. Continue the line $D\ P$ to the reservoir; the point $P\ H$ is the *pressure slope*. All of that head of liquid between the line $P\ H\ x$ and the exit (d) of the delivery tube is called the *pressure head* or *resistance head*. The head or stand of liquid below the line $P\ H\ x$ represents the quantity of potential energy which is made kinetic, and consumed in overcoming the resistance offered by the delivery tube.

What becomes of the potential energy represented by that portion of the water between $P\ H\ x$ and $V\ H\ y$? That energy is the source of the velocity with which the liquid jets from the end of the delivery tube. If one wishes to find the velocity he has only to use the distance $y\ x$ or the distance $y'\ D$ for h in the formula $v = \sqrt{2gh}$. The stand or head of liquid between $P\ H\ x$ and $V\ H\ y$ is called the *velocity head*.

The velocity head ($V\ H$) plus the pressure head ($P\ H$) is called the *driving head* ($P\ H + V\ H = D\ H$).

In studying the laws of the flow of liquid through tubes under constant pressure we have to consider the following factors: (α) driving head, (β) resistance head, (γ) velocity head, (δ) lateral pressure as indicated by the piezometers, (ε) resistance.

The solution of the following problems will throw much light upon the practical problems of the circulation: (I) What is the total effect of increasing or of decreasing the driving head (α)? (II) What is the effect of increasing or of decreasing the resistance (ε), the driving head remaining the same? (III) What is the effect of a simultaneous increase of (α) and increase of (ε)? (IV) The effect of a simultaneous increase of (α) and decrease of (ε)? (V) Decrease of (α) and increase of (ε)? (VI) Decrease of (α) and decrease of (ε)? (VII) How may (γ) be increased without increasing (α)? (VIII) How may (β) be increased without increasing (α)? (IX) What factors cause a variation of velocity? (X) Of lateral pressure?

(*c*) **The Velocity of the Flow** of a liquid through a tube has been defined as (α) *axial* and (β) *mean* and (γ) *mural*. The axial velocity is that attained by a particle swept along the middle of the stream. The mural velocity is that attained by a particle which moves along the wall of the tube, much retarded by friction of the liquid against the wall. The mean velocity is between these two, and approximately half the axial velocity. The mean velocity per unit time multiplied by the area of the tube equals the discharge in unit time.

b. The Flow of Liquids under Intermittent Pressure.

It is understood by intermittent pressure that the pressure shall be exerted in a rhythmical series of impulses, such as is observed in the working of a *pump*.

Intermittent Pressure through Inelastic Tubes.—If a pump ice the reservoir of Fig. 84, it will be found that the liquid will from the distal end of the delivery tube *in a series of jets* corre- iding to the action of the pump, and that the lateral pressure, as ated by the piezometers, will also vary with the action of the p, being highest at the moment that the liquid is being driven i the delivery tube with greatest force.

) **With Low Terminal Resistance** in the delivery tube the rise fall of pressure is moderately accentuated.

) **With High Terminal Resistance,** such as is afforded by a capil- tube at D, the rise and fall of the pressure within the delivery is greatly accentuated.

Intermittent Pressure through Elastic Tubes.—Instead of nelastic delivery tube use a thin rubber tube.

) **With Low Terminal Resistance** one notes no essential difference i previous observations with the inelastic tube.

) **With High Terminal Resistance,** however, there is a marked sformation in the character of the stream. It issues from the terminal capillary *not in jets, but as a continuous and, under rable circumstances, constant stream.*

ow is this accomplished? The sudden influx of liquid thrown the tube by the pump expands the tube, bringing into play its *icity.* When the pump reverses and the valve closes, the walls he tube contract upon the contents and force liquid out of the le while the pump is filling. If the pump acts quickly enough, jet from the nozzle of the delivery tube may be not only con- ous, but quite constant.

he quantity of liquid delivered from a capillary nozzle under i conditions is naturally much greater than the quantity delivered i the same capillary nozzle with an *inelastic* delivery tube. Other antages will be discussed later.

c. The Flow of Liquids Influenced by Other Factors.

) **The Size of the Tube.**—If there were no friction the size of tube would be of no consequence. The liquid which lies next he wall of the tube—*i. e.*, the liquid which wets the wall—does flow at all; the layer next to the wetting layer flows more slowly i any other layer, and the layer that is farthest from the wall of tube flows most rapidly.

'he middle, rapidly flowing current has friction against the next rnal less-rapidly flowing current, and thus a large portion of the tic energy may be expended in overcoming friction or resistance. urally the larger the tube the smaller the proportion of friction. may formulate the following law: *The resistance is in inverse ortion to the diameter of the tube.*

Further: *The resistance in a given tube increases with the velocity of flow.*

(*b*) **The Change of Course** through bending of the tube causes a change in the distribution of the resistance (greater in front of the bend and less beyond it), but does not affect the final discharge or velocity.

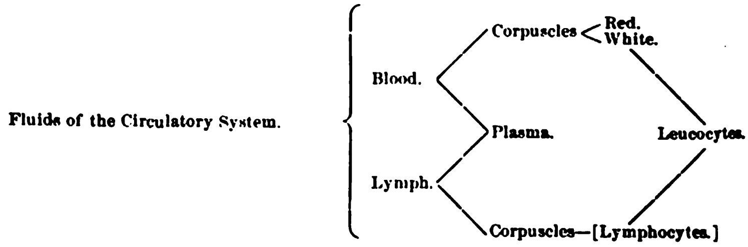
(*c*) **The Effect of Varying Lumen** is to cause a variation of the velocity with the varying lumen. Leonardo da Vinci, who was a great hydraulic engineer as well as a great painter, formulated this law: *The velocity of the current at any point is inversely proportional to its cross-sectional area.*

The cross-sectional area of the capillaries taken together equals 500 to 700 times the cross-sectional area of the aorta.

(*d*) **The Effect of Branching** is to introduce eddies and whirls into the stream. This causes increased resistance. If the ramification of the tubes leads to greater sectional area the velocity will decrease proportionally; if to smaller sectional area the velocity will increase proportionally.

THE PHYSIOLOGY OF CIRCULATION.

A. CLASSIFICATION OF THE FLUIDS, TISSUES AND ORGANS.



Tissues and Organs for the Formation or Destruction of Corpuscles.
- Red Marrow of Bones.
- Lymph Glands.
- Spleen.

Organs of Transmission of Fluids.
- Of Blood.
  - Heart.
  - Arteries.
  - Capillaries.
  - Veins.
- Of Lymph.
  - Lymph-radicles.
  - Lymphatics.

Organs of Control.
- Cranial Centers
  - Cardiac.
  - Vaso-motor.
- Parts of Vago-Sympathetic System.
- Vaso-Motor Nerves.

B. THE CIRCULATING FLUIDS.

The blood is called the vital fluid, not because it has any life within itself, but because it carries the food and oxygen, upon which the life of the cells depend, from the digestive tract and lungs to the active tissues. The amount of food which the blood contains is comparatively small, so that the whole volume of blood in circulation at any one time might be replaced by an artificial plasma without seriously injuring the animal, provided this artificial blood could be at once replenished with absorbed food from the digestive system. Thus, it is not so much the quantity of food in the blood at any one time as the quantity which it carries to the tissues during any given period, say, twenty-four hours, which gives the blood its importance.

In a similar way the blood contains at any one time only a comparatively small amount of oxygen, and this amount could be lost to the system and cause comparatively little disturbance, provided the source of supply would not be interrupted. The blood sustains to the organism the relation similar to that of any transportation system to society. The amount of matter in transit at any one time might be lost without seriously disturbing society, but the complete destruction and loss of the transportation system would at once introduce most distressing conditions.

We will get our clearest idea of the relation of the blood to the organism if we look upon it simply as a means of distribution of: (I) products of absorption from the alimentary tract; (II) oxygen; (III) products of tissue katabolism; (IV) carbon dioxide gas. These collected materials are transported from the point of collection to organs which are to utilize them or excrete them.

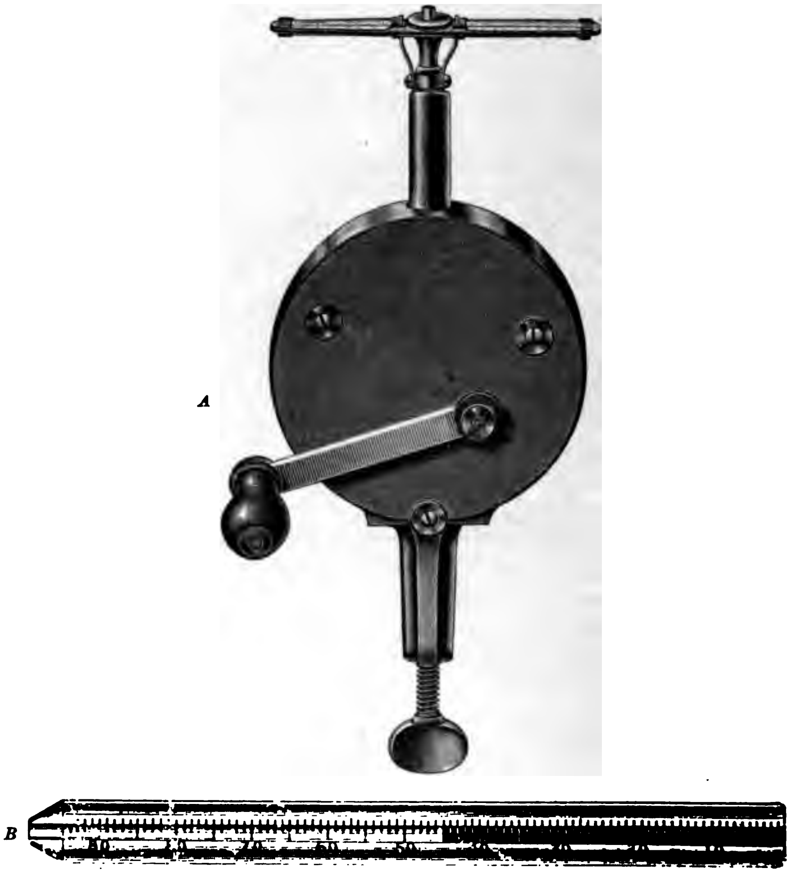
1. THE BLOOD.

I. THE PHYSICAL PROPERTIES.

1. **Physical Constitution of the Blood.**—*The blood is a liquid.* The fact that the blood is not transparent leads at once to the conclusion that it is not a homogeneous liquid, but that there are particles held in suspension. Johannes Müller succeeded in separating the liquid from the suspended particles by filtration. Before that time, however, the microscope had revealed the fact that the particles were corpuscles or cells—highly specialized cells, however. The liquid in which the *corpuscles* are suspended is called liquor sanguinis, or *plasma*. There are three methods of procedure in separating blood into its physical components:

(*a*) **By Filtration.**—Johannes Müller succeeded in filtering frog's blood after adding to it a small quantity of $MgSO_4$ or Na_2SO_4 or ½ per cent. sugar. He failed to filter mammalian blood after the same method; but Alex. Schmidt has done so repeatedly with horse's blood, if proper precautions are taken, instantly subjecting the drawn blood to 0° C., mixing with 20 per cent. of its volume of Na_2SO_4, and filtering after an hour or two.

FIG. 84

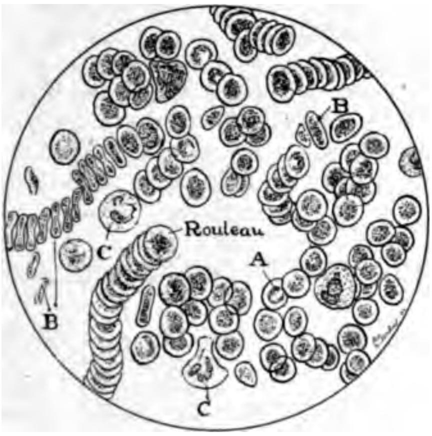


A. The hæmatocrit. The attachment at the upper end of the vertical shaft is made to rotate at a speed of 7000 to 10,000 per minute by means of the gear-work of the body of the instrument. Each arm of the rotating attachment is provided with a capillary tube, which is graduated into 100 divisions. If the tube be filled with blood and rotated for two or three minutes at the speed above mentioned, the corpuscles will be thrown to the outer end and the volume per cent. may be read off on the tube. *B*. An enlarged view of tube with centrifugalised blood.

(*b*) **By Subsidence.**—If the blood of a mammal—especially of a horse—be mixed, as above described, with 20 per cent. of its volume of saturated solution of $MgSO_4$ or Na_2SO_4 and subjected instantly to freezing temperature, it is found that the corpuscles will sink to the bottom, leaving the clear plasma above. This is facilitated by oiling the inner surface of the receptacle. If the conditions are very favorable the blood from the jugular vein of a horse may be separated without the addition of the salt solution.

(*c*) **By Centrifugation.**—If the blood of any animal be drawn into a capillary tube and instantly subjected to centrifugation, the heavier corpuscles are thrown to the outer end of the tube and the separated plasma and corpuscles may be quantitatively determined. Fig. 84 shows a centrifuge, or hæmatocrit; a speed of 7000 to 10,000 rotations per minute is sufficient to throw all the corpuscles to the outer end of the tubes in two or three minutes. The volume per cent. may be read off on the graduated capillary tube.

FIG. 85



Human red blood corpuscles, showing also rouleau formation.

2. **Color.**—The color of the blood in the body varies from light scarlet in the arteries to a dark bluish-red in the veins. The red color is due entirely to the red corpuscles. Owing to the physical properties mentioned above the blood is opaque—even thin layers of it obstructing the light. The bright-red color of the albino's eyes is due to the blood of the central artery of the retina—unobstructed from view by the translucent iris. The pink color of the lips, nails, conjunctiva, and oral mucous membrane in health is due to the blood. If the blood has a smaller number or a poorer quality of red corpuscles, the pink gives place to a pale or even waxy-white color; while in asphyxia and certain serious heart lesions these parts take on a ghastly bluish color.

3. **Odor.**—The peculiar odor of freshly shed blood is well known. This odor is somewhat different in the blood of different animals,

and is due to the presence in somewhat varying relative amounts of volatile fatty acids. The odor of human blood is less strong than that of most animals. In blood which has been shed for some time the odor may be revived by liberating these volatile fatty acids with concentrated H_2SO_4.

4. **Taste.**—Blood has a saline taste, due to the salts dissolved in the plasma.

5. **Specific Gravity.**—The specific gravity of the blood as a whole is 1056 to 1059 in man, and 1051 to 1055 in woman; in children it is less, and is subject to greater variations. This is a composite specific gravity made up of plasma 1007 and blood corpuscles 1105. It is due to this difference in the specific gravity of the plasma and corpuscles that separation by sedimentation or by centrifugation is possible. The density of the blood is due almost entirely to the iron in the corpuscles. As the specific gravity of the blood has some clinical importance it may be determined as follows: Take a mixture of benzole 889 and chloroform 1526 of a specific gravity of 1060 in a cylinder and place a drop of fresh blood in it. If the blood is lighter than the mixture it will rise to the top and if heavier it will sink. Add, then, either chloroform or benzole until the blood remains at the centre of the mixture. The specific gravity of the mixture will be that of the blood, and may be determined with a specific gravity bulb.

II. THE MORPHOLOGY OF THE BLOOD.

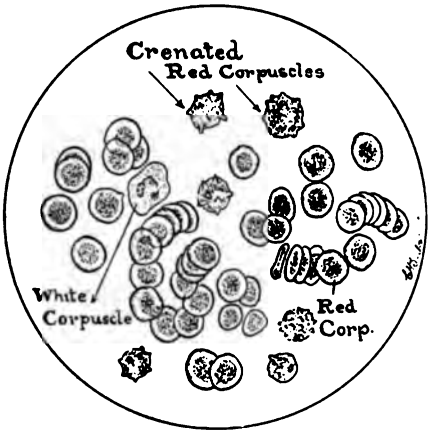
a. The Red Blood Corpuscles.

1. **Form.**—The red blood corpuscles are circular, biconcave, elastic, non-nucleated disks. They are about 7.7 microns in diameter and 1.9 microns in thickness near the periphery; the thickness in the centre of the disk is less (Fig. 85). This accounts for the microscopic appearance of a nucleus in the centre of the disk (Fig. 86). When viewed with the microscope the rim of the corpuscle appears light, while the centre appears dark, because the latter is out of focus. Now, by carefully moving the objective downward the centre of the corpuscle will appear light and the rim will appear dark, and this is another proof that the centre of the corpuscle is thinner than the periphery.

If the film of fresh blood is deeper than the diameter of the corpuscles and the glass on which it is spread is jarred or shaken, the disks readily form into rouleau like piles of coins (Fig. 85). The cause of this formation is probably due to the biconcave shape and not to any inherent quality, as has been supposed. If blood is exposed to the air for a short time, or if the plasma be diluted with a hyperisotonic fluid—*i. e.*, a fluid of greater density than the plasma

—the red blood corpuscles become crenated; that is, the corpuscle shrinks and the surface is puckered, giving the corpuscle the appearance of containing foreign bodies in its protoplasm. This is especially realistic when the corpuscles are just beginning to crenate and are moving or rolling about the microscopic field (Fig. 86). If, on the other hand, the plasma be diluted with a hypisotonic fluid—*i. e.*, of less density than the plasma—the corpuscles at once swell and assume a nearly spherical form, finally becoming quite spherical. If pure water be used the hæmoglobin will be gradually dissolved and the corpuscles appear bleached out. This is called laky blood. The corpuscles may be stained with the ordinary stains by placing a thin film of fresh blood upon a cover-glass, and fixing it by heating at 100° C. or immersion in absolute alcohol for a few minutes. The best stains are a 1 per cent. aqueous eosin in 50 per cent. alcohol and 10 per cent. methylene blue in 50 per cent. alcohol, and the Ehrlich triple stain.

FIG. 86



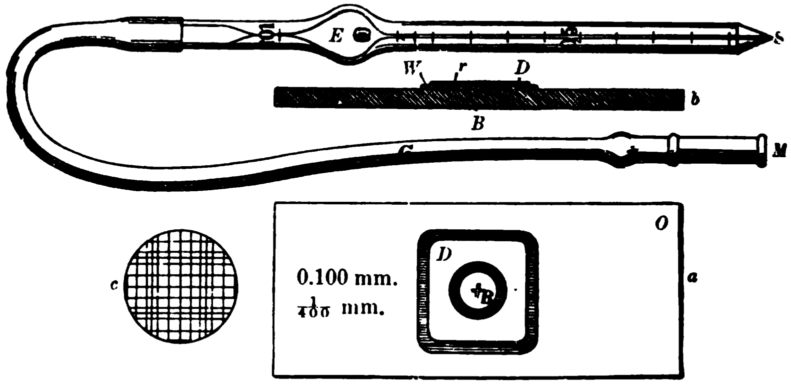
Red blood corpuscles showing crenation.

2. **Size.**—There are two methods of determining the size of a microscopic object: (I) Its image may be projected upon a scale by a camera lucida and the dimensions determined. (II) A much more convenient method is to measure directly, objects in the field of the microscope, with the aid of an eye-piece micrometer. By one or the other—usually the latter—of these methods the average diameter of the red blood corpuscles has been determined, and is 7.7μ, or 7.7 micromillimetres (a micromillimetre is one one-thousandth of a millimetre). There is little variation in the size, more than 90 per cent. of the corpuscles being very near to the average. The remaining more variable corpuscles, however, extend the limits of

size to 6.7μ for the minimum and 9.3μ for the maximum. The maximum thickness of a red blood corpuscle is about 1.9μ. The size is somewhat diminished by septic fever, asphyxia, or the administration of considerable morphine; and is increased by alcoholism, quinine, or watery condition of the blood. The size of the red blood corpuscles has had considerable medicolegal importance; but the fact that the corpuscles of animals frequently associated with man fall within the limits of variation of human corpuscles has led to a general distrust of this evidence. The average diameter of the red blood corpuscles of a dog is 7.3μ (varying from 6.6μ to 9μ), of a cat 6.5μ and of a rabbit 6.9μ.

3. **Number.**—The normal average of red corpuscles per cubic millimetre of blood is in man 5,000,000 and in woman 4,500,000. The total number may be estimated by actually counting the number in a measured amount of accurately diluted blood. The variations that occur in health are quite small and are due to normal processes. A variation between 6,000,000 and 4,000,000 is considered practically normal. Any deviation from the normal quickly causes a diminution in the number, size, and the quality of the red blood corpuscles; in fact, simple, unhygienic surroundings or habits speedily cause these changes without other demonstrable pathological conditions.

FIG. 87



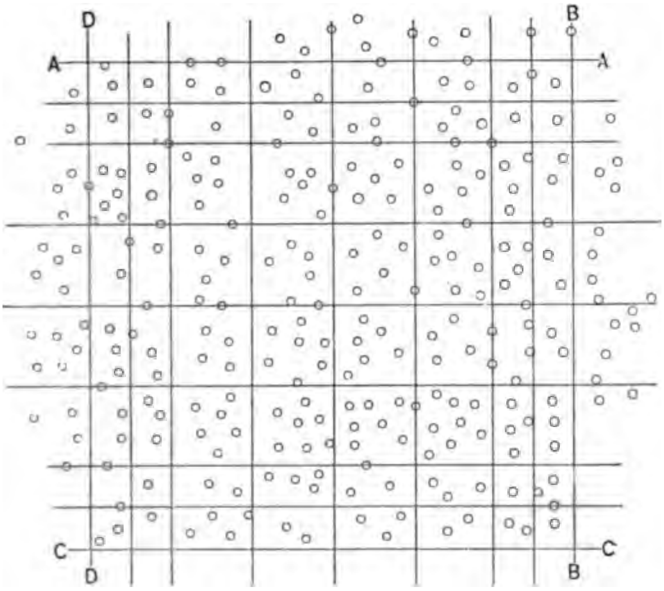
The Thoma-Zeiss blood counter. The mixing pipette in which each volume of blood is diluted to 100 to 200 volumes. *a*, *b*, and *c*, plan and elevation of the counting slide.

In a man weighing 65 kilos there are about 5 kilos of blood, or $\frac{1}{13}$ of the entire weight. Then there would be approximately 25,000,000,000,000 red blood corpuscles in man. The life of a red blood corpuscle is not known, but it is variously estimated to be from two to four weeks. At any rate it means that billions of red blood corpuscles must be formed every day. It will be readily seen that such an immense process which depends upon assimilation and elimination (anabolism and katabolism) is easily disturbed.

The number of corpuscles per unit volume can be quite accurately counted with the Thoma-Zeiss hæmacytometer. The use of this instrument involves the accurate dilution of the blood and the actual counting of the corpuscles in a definitely measured microscopic space.

The diluting pipette consists of a capillary tube and a bulb, the latter holding 100 volumes of fluid while the former holds 1 volume. The ruled slide is marked on its upper surface into 400 squares $\frac{1}{20}$ mm. each way with extra lines in every fifth row to enable one to locate any group of squares. Around the marked area is a groove, and then a frame raised $\frac{1}{10}$ mm. above the marked plate, thus making between the cover-glass and the ruled plate a cubic space $\frac{1}{20}$ mm. $\times$ $\frac{1}{20}$ mm. $\times$ $\frac{1}{10}$ mm, or $\frac{1}{4000}$ c.mm. To make the count, fill the capillary tube with fresh blood to the mark "1," then draw up the blood and the diluting solution (1 per cent. NaCl or 5 per cent. Na_2SO_4) to the mark "101," then thoroughly mix the blood and the diluting solution in the bulb, and place a drop of this mixture on the marked slide. Then with the microscope count the corpuscles in a number of cubic spaces to get the average and make the correction for dilution, *e. g.*, twelve corpuscles per cubic space $\times$ 4000 $\times$ 100 = 4,800,000 red blood corpuscles per cubic millimetre. In any particular specimen of blood the number of red corpuscles per cubic millimetre

FIG. 88



Appearance of slide under about 500 diameters' magnification. One counts all corpuscles which lie upon the right and lower boundaries of each square.

will vary with varying proportions of plasma and corpuscles. It follows, then, that anything which tends to increase the volume of the blood plasma will decrease the number of corpuscles per cubic millimetre of blood; while anything which tends to decrease the volume of the plasma will increase the number of corpuscles per cubic millimetre of blood—*i. e.*, the relative number of red blood corpuscles varies inversely as the amount of plasma. The relative number of red blood corpuscles will be increased by the passage of the blood through cutaneous arterioles and capillaries, after use of solid food, and after free perspiration, diuresis, or diarrhœa. The relative number of red blood corpuscles will be decreased by the passage of the blood through intestinal capillaries after a fluid meal; also by any causes leading to sudden decrease in perspiration or in excretion of water from the kidneys.

If the corpuscles do not vary in size it is clear that in successive examinations of the blood of the same individual the proportions of blood corpuscles found by centrifugation will be approximately proportional to the number per cubic millimetre. If the corpuscles vary in size the number will not be proportional, an increase in number being accompanied by a corresponding decrease in size.

b. The White Blood Corpuscles, or Leukocytes.

These cells are composed of unmodified protoplasm and possess a nucleus. They are wholly unspecialized and are the potential equivalents of a primitive unicellular animal—*e. g.*, the amœba. They are identical with the lymph corpuscles and with the wandering connective-tissue cells. In summing up their physical and morphologic characters Landois says: "These cells consist of more or less spherical masses of protoplasm which is sticky, highly refractile, soft, mononucleated or multinucleated, capable of amœboid movement, and devoid of an envelope (cell membrane)." They are of different sizes, from 8μ to 14μ in diameter, and are classified as follows: (See Plate I., Fig. 1.) (I) *Small mononuclear,* 8μ to 10μ in diameter, comprise 20 to 30 per cent. of the leukocytes. (II) *Large mononuclear,* 12μ to 13μ, and 4 to 8 per cent. (III) *Polynuclear, (a) neutrophile,* 12μ to 14μ, and 60 to 70 per cent.; *(b) eosinophile,* 12μ to 14μ, and ½ to 4 per cent. They vary normally in number from 6000 to 15,000. These variations are mostly due to the process of digestion. The usual average, however, is about 8000 or 10,000 per cubic millimetre. This count may be made while counting the red corpuscles by adding 5 per cent. of alcohol methyl violet to either of the diluting solutions, thus making the white corpuscles show by staining their nuclei. Or the white corpuscles may be counted alone by using a ½ per cent. solution of acetic acid, thus destroying the red corpuscles and making the white corpuscles more distinct.

Fig. I

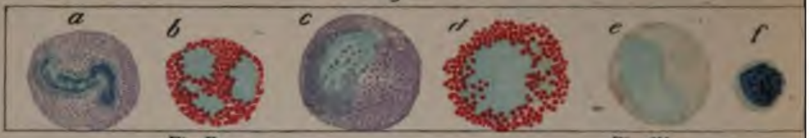


Fig. II.

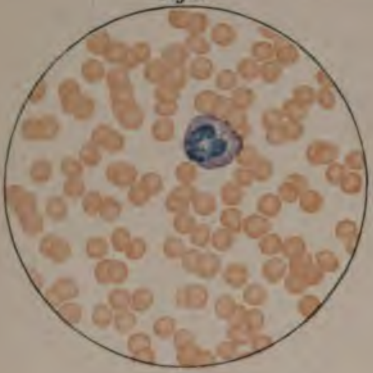


Fig. III

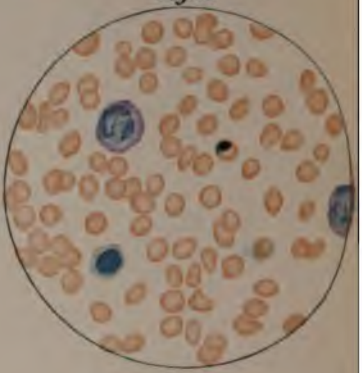


Fig. IV.

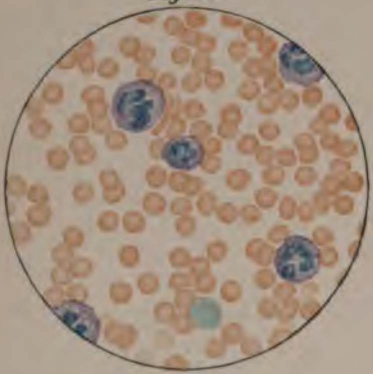


Fig. V.

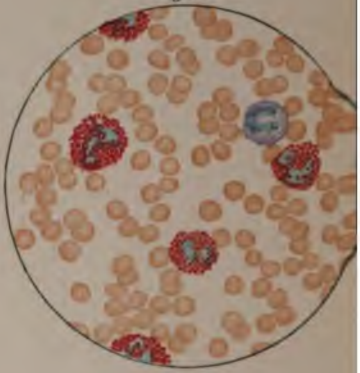


Fig. VI.

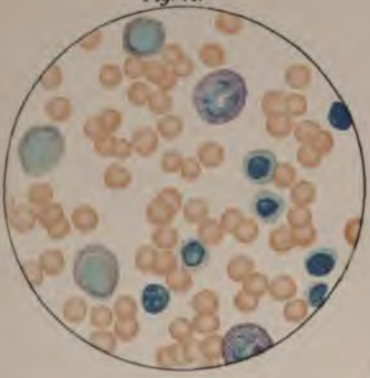


Fig. VII.

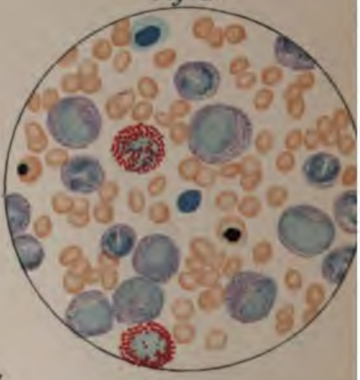
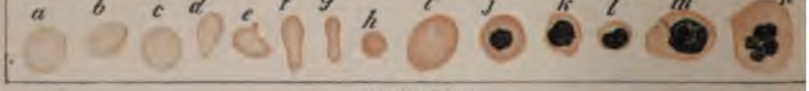


Fig. VIII.



DRAWN BY J.N.Z. CHASE

PLATE I.

BLOOD.

(Ehrlich triple stain.)

(Prepared by Dr. I. P. LYON.)

Fig. I. TYPES OF LEUCOCYTES.

a. Polymorphonuclear Neutrophile. *b.* Polymorphonuclear Eosinophile. *c.* Myelocyte (Neutrophilic). *d.* Eosinophilic Myelocyte. *e.* Large Lymphocyte (large Mononuclear). *f.* Small Lymphocyte (small Mononuclear).

Fig. II. NORMAL BLOOD.

Field contains one neutrophile. Reds are normal.

Fig. III. ANÆMIA, POST-OPERATIVE (secondary).

The reds are fewer than normal, and are deficient in hæmoglobin and somewhat irregular in form. One normoblast is seen in the field, and two neutrophiles and one small lymphocyte, showing a marked post-hæmorrhagic anæmia, with leucocytosis.

Fig. IV. LEUCOCYTOSIS, INFLAMMATORY.

The reds are normal. A marked leucocytosis is shown, with five neutrophiles and one small lymphocyte. This illustration may also serve the purpose of showing the leucocytosis of malignant tumor.

Fig. V. TRICHINOSIS.

A marked leucocytosis is shown, consisting of an eosinophilia.

Fig. VI. LYMPHATIC LEUKÆMIA.

Slight anæmia. A large relative and absolute increase of the lymphocytes chiefly the small lymphocytes) is shown.

Fig. VII. SPLENO-MYELOGENOUS LEUKÆMIA.

The reds show a secondary anæmia. Two normoblasts are shown. The leucocytosis is massive. Twenty leucocytes are shown, consisting of nine neutrophiles, seven myelocytes, two small lymphocytes, one eosinophile (polymorphonuclear) and one eosinophilic myelocyte. Note the polymorphous condition of the leucocytes, *i.e.*, their variations from the typical in size and form.

Fig. VIII. VARIETIES OF RED CORPUSCLES.

a. Normal Red Corpuscle (normocyte). *b, c.* Anæmic Red Corpuscles. *d-g.* Poikilocytes. *h.* Microcyte. *i.* Megalocyte. *j-n.* Nucleated Red Corpuscles. *j, k.* Normoblasts. *l.* Microblast *m, n.* Megaloblasts.

The diluting pipette best suited for the white corpuscle dilution dilutes the blood only ten times, thus giving a more accurate count by not diluting the blood so much.

The number of white corpuscles is increased during pregnancy, after parturition, and is very much decreased by fasting.

The abnormal increase in the relative number of leukocytes is characteristic of the disease *leukæmia;* and may be associated with other affections of the blood or blood-forming organs.

The minute structure of the leukocyte is not revealed to the eye without the use of some system of differential staining. To Ehrlich we are indebted for the first systematic work in this field. He found that granules in the cytoplasm reacted differently to acid, neutral and basic stains. The granules which take the acid stain, eosin, he called *eosinophiles,* those which take the neutral dyes he called *neutrophiles,* and so on, differentiating different classes of granules. As the subject was studied it was found that classification of the leukocytes, according to their reaction to the stains, is convenient and valuable clinically. The term eosinophile and neutrophile has come to be applied to the leukocyte and not to the granules alone. The most common leukocyte is the polymorphonuclear neutrophile, or simply *neutrophile;* also found sparingly in normal blood is the *eosinophile.* The accompanying plate gives the varieties of leukocytes.

There may be an abnormal proportion of the normal leukocytes or there may be an appearance, in considerable numbers, of the rarer forms of leukocyte. This subject is discussed *in extenso* in the clinical treatises on the blood.

c. Other Structural Elements of the Blood.

1. **Blood Platelets of Bizzozero** are "pale, colorless, oval, round, or lenticular disks of variable size"—average 3μ—whose origin, function, and destiny are yet under discussion."

Lilienfeld[1] regards the substance of blood plates as belonging to the nucleoalbumins. They may be observed in a specimen of blood obtained by placing a drop of ½ or 1 per cent. osmic acid on the finger and pricking through the drop, mixing the drop of blood and acid at once. The plates disintegrate directly after the shedding of blood, and inasmuch as the microscope reveals little clumps of the granular debris of the plates where the fibrin fibrils cross, the theory that these problematic bodies are active agents in coagulation seems to have a justifiable basis. The part they play is probably to furnish one source of the fibrin ferment.

2. **Elementary Granules** are minute particles of proteid matter probably arising from the disintegration of white corpuscles or of the blood platelets.

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[1] Zeit. phys. Chem., Bd. xx. p. 155.

d. Plasma.

The plasma is an alkaline, viscid, light straw-colored fluid containing various salts in solution. It has a specific gravity of about 1007, which can be obtained from the plasma collected from the blood after subsidence of the corpuscles. The plasma comprises about 50 per cent. of the blood.

III. THE CHEMICAL PROPERTIES OF THE BLOOD.

a. Chemical Composition.

1. **Analysis of the Blood** proves it to be composed of 775 to 800 parts of water and 200 to 225 parts of solids. The solids are 192 to 217 parts of organic and 7 to 8 parts of inorganic matter. The organic matter is composed of hæmoglobin, of proteids, fats, and traces of sugar, while the inorganic matter is composed of NaCl, KCl, $NaHCO_3$, Na_2HPO_4, $CaHPO_4$, $CaSO_4$, $MgCl_2$, etc.

The best idea of the chemical composition of the blood as a whole may be obtained by first separating the blood into plasma and corpuscles by centrifugation, and then analyzing each separately. Human blood so treated would give approximately the results recorded in the following table, which is the result of an analysis reported by Halliburton:

Chemical composition of blood.	Plasma av. 50%. Max. 567. Min. 456. Take 100 parts.	Water						90.29%
		Solids 9.71%	Organic 8.86%	Proteids	Serum albumin Serum globulin			7.9 %
					Fibrin			0.4 %
				Extractives: [Fat, dextrose, urea, kreatin, purin bases, etc.]				0.56%
			Inorganic 0.85%	Soluble salts.	NaCl KCl $NaHCO_3$ Na_2HPO_4			0.85%
				Insoluble salts.	$CaHPO_4$ $CaSO_4$			
								100.00
	Corpuscles. Av. 50% Max. 54.4% Min. 43.3 % Take 100 parts.	Water						68.80%
		Solids 31.2%	Organic 30.4%	Proteids 29.79%	Hæmoglobin 27	Hæmatin	Fe.	27.36%
						Globulin		
					Globulin			2.43%
				Fats	Lecithin Cholesterin			0.61%
			Inorganic 0.8%	KCl NaCl $MgCl_2$ $CaHPO_4$ $Mg_3(PO_4)_2$				0.80%
				Fe. [See Hæmatin.]				
								100.00

2. **Reaction.**—The reaction of the blood arises not from any peculiarity of the corpuscles, but from the plasma. This fluid is a complex one and among other constituents contains Na_2HPO_4 and $NaHCO_3$, which give it an alkaline reaction in freshly shed blood; but shed blood rapidly loses its alkalinity.

The average alkalinity of the blood is equal to that of a 0.2 per cent. solution of sodium hydrate. The reaction of the blood may be qualitatively determined by placing a drop upon the surface of a plaster-of-Paris disk, which has been impregnated with neutral litmus. If after a moment's contact the blood be wiped off, the faint blue will be seen. The alkalinity of the blood may be decreased during health by (I) great muscular exertion, and (II) by exposure of the blood to the conditions of coagulation. Patbologically the alkalinity of the blood may he *increased* by persistent vomiting, and *decreased* by (I) anæmia, (II) uræmia, (III) rheumatism, (IV) high fever, (V) diabetes, (VI) cholera.

"Generally speaking, the ammonium salts which are formed within the body appear in the urine as urea, but aside from their importance in this respect they represent a reserve of alkali which is capable of preventing an undue diminution in the alkalinity of the blood by vicariously taking the place of the fixed alkalies. This vicarious action is normally also at work, but is then comparatively insignificant in extent. If, however, a specially large demand is made upon the alkalies of the body, as when mineral acids are ingested for experimental purposes, the vicarious action of the ammonium salts at once enters into play. Unless carried to extremes, the alkalinity of the blood, in the carnivorous animals at least, remains constant, but the elimination of urea is proportionately less, and the deficit of nitrogen in this form appears as ammonia in combination with acids.

"By gradually increasing the amount of acid it is thus possible to bring about the almost complete disappearance of urea from the urine. A point, however, is finally reached when the animal succumbs to acid intoxication, and then, and not before, may free acids appear in the urine. Death in such cases resnlts from suffocation, as there is not sufficient alkali left in the lymph and plasma to combine with the carbon dioxide in the tissues." (Simon, *Physiological Chemistry,* p. 231.)

The quantitative determination of the degree of alkalinity of the blood becomes a matter of some clinical importance. The chemical composition of the blood is remarkably constant considering the complexity of its composition and the complexity of the processes involved in its rejuvenation and the complexity of the processes which free it of waste products. Through excess of inorganic salts in the food a temporary excess of those salts may exist in the blood; but the increased endosmosis of fluids and the increased excretion of urine and perspiration very soon carry off the excess of salts and water and restore equilibrium.. Excess of fats and carbohydrates is deposited in the form of fat, thus restoring very readily the equilibrium in the blood, but leading eventually to an excess of fat deposit in the system.

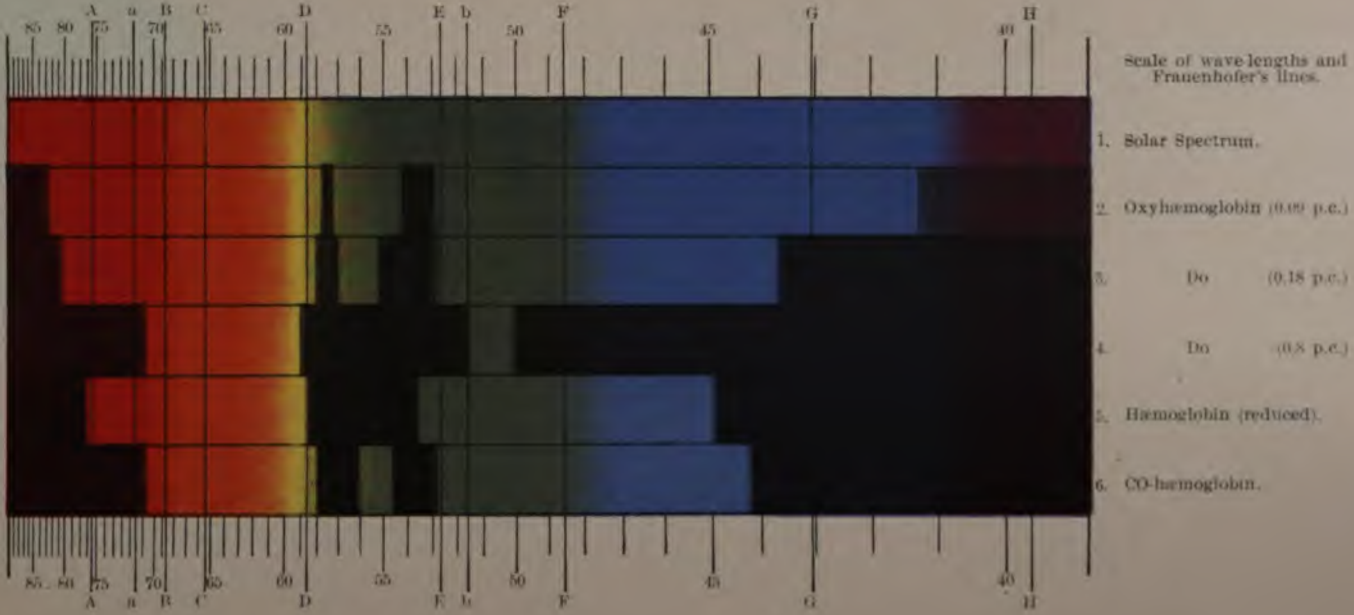
Excess of proteids may be broken up, fats formed from the carbonaceous portion and deposited in that form. On the other hand, a deficient supply of any of these may be for a short time overcome by the use of reserve materials; but sooner or later the deficiency will manifest itself in various disturbances of the general nutrition. Experience has proven that the constituent of the blood most important, from a clinical standpoint, is the hæmoglobin. The only function of hæmoglobin is to transfer oxygen *from the lungs*—the seat of external respiration—*to the cells*—the seat of internal respiration; and though the plasma assists in this function it is quite insufficient alone, and in fact a small decrease in the hæmoglobin is soon attended by a disturbance in general nutrition through lack of a proper supply of oxygen to the active cells—*i. e.*, cells of secretion and excretion as well as muscle and nerve cells. Moreover, the important part that iron plays in the functions of hæmoglobin, the great difficulty with which iron is assimilated, together with the important proteid constituents of hæmoglobin, make that compound a most sensitive and reliable index of the general nutrition both as to organic and inorganic compounds. It is, then, a matter of the greatest clinical importance to be able to determine with reasonable accuracy the amount of hæmoglobin present in the blood.

b. Quantitative Determination of Hæmoglobin.

1. **Gravimetric Method.**—The red blood corpuscles are made up of stroma and hæmoglobin. The stroma is the small framework of the corpuscle. Hæmoglobin comprises about 90 per cent. of the corpuscle, and is made up of 96 per cent. proteid and 4 per cent. hæmatin. It therefore follows that the quantity of the iron in the ash of a weighed quantity of blood is an exact index of the quantity of hæmoglobin present. This method is very valuable for certain physiologic investigations, but the time required to make a quantitative estimation of the iron is too great to justify this method for clinical use.

2. **Spectroscopic Method.**—(*a*) It has been found that sunlight or lamplight in passing through diluted blood entering before the slit of a *spectroscope* suffers an absorption of a part of the yellow and a part of the green of the spectrum; and the latter appears with two black bands through those colors—one just at the right of the D lines and a broader one just at the left of the E line (Plate II.). It has been further discovered that a quantitative variation of the hæmoglobin causes a broadening of these bands. Preyer has used

PLATE II.



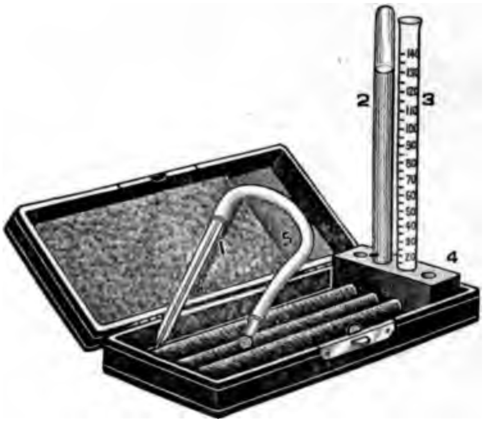
Showing Spectra of Hæmoglobin in certain Qualitative and Quantitative Variations.

(After Schaefer. Text-book of Physiology, vol. i, p. 208.)

basis for a quantitative determination for clinical purposes. ımpanying plate shows, in spectra 2, 3 and 4, the influence ring quantity of hæmoglobin upon the transmission of light risms. An 0.8 per cent. solution of hæmoglobin absorbs the light, while a solution one-tenth that strength would ttle light; namely, the two extremes of red and violet and acteristic bands in the yellow and green. Study carefully ion and width of these absorption bands.

variation of this method which gives much more exact described in Long's *Chemical Physiology* (pp. 150 to 156). ıethod the *spectroscope* is converted into a *spectrophotometer* quantity of light transmitted is measured, the basis of the ation being the fact that equal dilutions of hæmoglobin equal amounts of light.

FIG. 89



Gowers' hæmoglobinometer.

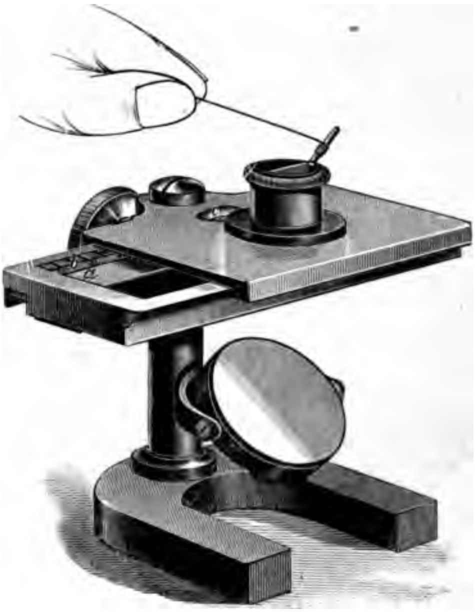
orimetric Methods of Determining the Hæmoglobin.— nation of the coloring matter of the blood is based on the fact that the healthy individual under normal surround- a normal amount, or 100 per cent. of coloring matter.

ischl's Hæmometer (Fig. 90) consists of a colored-glass ıd a partitioned cup in which distilled water and definitely ılood are placed on either side. The comparison is then ectly in percentages by the use of transmitted artificial light.

wers' Hæmoglobinometer (Fig. 89) consists of a standard olution, a pipette holding 20 c.mm., and a graduated test- he colored solution represents the color of a 1 per cent. of normal blood. The graduated tube is marked in 100 or ıal parts; each mark represents 20 c.mm. To make the lace 20 c.mm. of blood in the tube and then dilute with distilled water until the color of diluted blood corresponds with that of the standard solution. Then read the percentage of coloring matter in the specimen from the graduated tube. There is one instrument for artificial light and another for sunlight; the former has a black pigment in the standard tube, the latter a white substance.

(*c*) Among the valuable instruments which should be mentioned are: **Oliver's**, which is like the Fleischl instrument, except reflected light is used. It is a very accurate instrument, but costly and hard to use. **Dare's**, which is the same as Fleischl's except it compares a film of undiluted blood with a colored-glass wedge. **Tallquist's** which compares undiluted blood in filter-paper with graduated red-colored paper.

FIG. 90



Fleischl's hæmometer.

IV. THE FUNCTIONS OF VARIOUS PARTS OF THE BLOOD.

a. Plasma.

This part of the blood carries in liquid form the nutriment of the body. The nutriment enters the alimentary canal in the form of various liquid or solid proteids, carbohydrates, and fats, with salts, solid or in solution in water. During digestion the proteids are changed to peptones, the carbohydrates to soluble s, the fats to fatty acids and soaps, and the salts are dissolved t the nutriment absorbed is much more uniform in both physical hemical properties than was the food.

ring absorption the peptones are changed to serum globulin erum albumin; the fatty acids and soaps are changed to emul- Soon after absorption the sugars are deposited as glycogen liver or consumed in the muscles; the fats are likewise disposed t the plasma is kept fairly uniform in the quality of its nutriment. nctions are: (I) to carry absorbed nutriment to the metabolic s; (II) to carry excrement to the organs of excretion; (III) to in carrying oxygen to the tissues and in carrying CO_2 from s to lungs.

b. Corpuscles.

The Red Blood Corpuscles.—These modified cells are *oxygen rs.* The oxygen is held chemically by the hæmoglobin and d from the lung capillaries to the metabolic tissues, where it t as essential as the nutrients.

The White Blood Corpuscles.—(I) These cells carry solid par- from one part of the organism to another. (See Decay and uction of Red Blood Corpuscles.) (II) They fill breaks in the uity of tissues and, with fibrin, build new tissue into the wound. They surround foreign bodies (*e. g.*, slivers), protecting the tissues extensive laceration. (IV) The leukocytes act as the scavengers, ting the organism as far as possible from the invasion of genic microbes. These are usually engulfed, digested by the ytes, and expelled from the system. This is called *phagocytosis.* eukocytes have also the power of being drawn to or of being ed from certain chemical and bacterial products; this is called *taxis.* (VI) The leukocytes have also the power of forming xins or bacterial poisons, to neutralize bacterial toxins if not stroy the bacteria themselves.

V. THE TOTAL QUANTITY OF THE BLOOD.

cases of severe hemorrhage, where the quantity of blood lost e more or less accurately determined, it may be important to the total amount of blood in the body in order to estimate roportion that has been lost. There are two methods for deter- g the total quantity of blood.

The Determination in a Dead Animal.—Welcker's (*Zeitsch. ionale Medicin,* 1858) method is as follows: (I) Bleed the l, taking the weight of the blood so obtained. (II) Of the first drawn, defibrinate a few grams to dilute and use as a standard. (III) Wash out the circulatory system with warm normal saline solution, determining the blood by diluting the standard with a measured quantity of water to the same color. (IV) Remove and hash all tissues, making an aqueous extract, whose blood content may be determined as in (III). The sum of amounts (I), (III), and (IV) is the total. This varies somewhat for different animals; usually from $\frac{1}{12}$ to $\frac{1}{19}$ of the body weight, averaging $\frac{1}{13}$ in man and the dog, $\frac{1}{14}$ in the cat, $\frac{1}{19}$ in the rabbit and in the newborn child.

2. **The Determination in a Live Animal.**—This was accomplished by Gréhant and Quinquand (*Jour. de l'anat. et physiol.*, etc., Paris, 1882, No. 6, p. 564), by allowing the animal to respire a known quantity of CO with oxygen, afterward determining the amount of CO in a small amount of drawn blood. Then, *Total blood : Drawn blood : total CO : : drawn CO.*

VI. THE PROTECTION OF THE BLOOD SUPPLY.

If the blood plays such an important part in the economy of the body, may we not expect that some provision is made for the protection of animals, in a measure at least, from accidental breaks in the integrity of the system of tubes in which the blood circulates? If any slight accident may sever an artery from which the blood can flow unhindered, then surely would animal life be precarious. But there have arisen in the animal kingdom two methods of protection against the accident indicated above.

1. **The Location of the Vessels.**—*All important vessels are located as deeply as possible.* Those that come near the surface are on the inner and flexor sides of the limbs, where there is greatest protection.

2. **The Influence of the Intima.**—Many small vessels, both veins and arteries, lie near the surface of the body. What special provision is made for these? The inner coat of a severed small vessel either mechanically or by some ferment influence is a most important factor in the ready formation of a clot.

3. **The Coagulation of the Blood.**—The most important protection against excessive bleeding is the tendency of the blood to undergo a change as soon as it passes through a wound in a vessel. This remarkable change which the blood undergoes involves a chemical reaction between certain constituents of the blood; the wonderful feature about this reaction is the fact that normally it is *adjusted* in *time* and *place* to the severing of the continuity of a bloodvessel.

The coagulation of normal blood is a phenomenon that takes place quite constantly in from three to five minutes, but in disease this may be prolonged indefinitely. The time required for coagulation may be approximately tested by placing a fresh drop of blood on a warmed glass slide, and while holding it in the hand draw through the drop a fine needle or a straw from an ordinary broom every quarter of a minute, and note when the clot follows the straw out of the drop.

The principal gross phenomena of coagulation, as observed in a beaker of drawn blood, are: (I) the formation within two minutes of a jelly-like layer over the surface of the blood; (II) the formation of a similar layer within two to seven minutes around the sides of the vessel; (III) the formation of a complete homogeneous clot in from seven to sixteen minutes; (IV) the contraction of the clot, which results in the exudation of serum from its surface. Eventually the contraction is so extensive that the clot occupies about one-half of the entire volume, and usually rests upon the bottom of the dish. *The time required* to completely coagulate the blood is, in man, two to sixteen minutes; in the horse, five to thirteen minutes; in the dog, one-half to three minutes; in the rabbit, one-half to one and one-half minutes. In the pigeon the coagulation is almost instantaneous.

Coagulation is hastened by: (I) temperature above normal body temperature; (II) contact with foreign matter; (III) agitation; (IV) addition of calcium salts.

Coagulation is retarded or prevented by: (I) low temperature; (II) addition of an equal volume of saturated solution of $MgSO_4$ or Na_2SO_4; (III) addition of oxalates, which precipitate the calcium as an oxalate; (IV) addition of leech extract; (V) injection of solution of commercial peptones into the vascular system of an animal before an experiment will retard coagulation.

4. **The Factors of Coagulation.**—These are some of the questions which have presented themselves for solution in this connection:

(1) What constituents of the blood take part in the reaction?

(2) Whence are these constituents derived?

(3) What are the factors which determine the time and place of coagulation?

All of these questions have been variously answered by various investigators. A review of the history of this investigation would consume too much time. Of the long list of students of these questions the name of Alexander Schmidt, who for over thirty years has been experimenting in this field at the Physiological Laboratory of Dorpat University, Russia, stands in the front rank. The Swedish investigator Hammarsten stands next in rank to Schmidt in this field. Alexander Schmidt's original theory published in 1861 was: *Fibrinogen, Fibrinoplastin* and *Fibrin Ferment* are the three fibrin factors, and their combination is determined in time and place by the liberation of the ferment at the point of rupture of the endothelial lining of the bloodvessels from leukocytes and endothelial plates. Hammarsten and Schmidt have more recently found that fibrinoplastin is not a necessary factor. Hammarsten and the Dorpat School have further found that "unless a certain amount of salts be present coagulation takes place slowly or only partially." Freund has shown that "the process of coagulation is always accompanied by an excretion (separation) of phosphates of the alkaline earths.[1] Fibrin contains a constant amount of these phosphates. Coagulable fluids coagulate after the addition of these salts. This is true, too, of sulphates of these metals—*e. g.*, $CaSO_4$." The theory of Wooldridge deserves mention here only to afford an opportunity to quote Halliburton's statement regarding it: "1. The whole theory is based upon experiments with peptone plasma; but such plasma performs differently from normal plasma. 2. It is difficult from Wooldridge's publications to find a logical basis for his conclusions." This statement was made ten years subsequent to the publication of the theory. Hammarsten's theory published in 1891 is, briefly stated, as follows: Coagulation is caused by *Fibrinogen* and Fibrin Ferment in the presence of neutral salts of the alkaline earths, especially $CaSO_4$ and $CaHPO_4$.

To Alexander Schmidt and the Dorpat School we must give the credit of making the most profound investigation of this subject. Most writers do Schmidt the injustice of only associating his name with the first theory which he published in the first years of his work, wholly ignoring all his subsequent investigations and the subsequent recasting of his theory. His publication in 1892 on *Blut lehre* is the most comprehensive treatise ever published on coagulation. Every step of the theory is based upon repeated experiment upon perfectly normal blood. Schmidt emphasizes the fact that coagulation is brought about by the action of a *ferment* upon the *fibrinogen*, both of which exist in the blood. He further emphasizes the necessity of the presence of the calcium salts. His investigation, however, does not stop at this point; he and his pupils have sought the source of the fibrin factors and find that not in the blood corpuscles, not in the blood platelets, and not in the endothelial cells alone is found the source of fibrin ferment, but that it arises wherever protoplasm undergoes destructive metabolism; and concludes, finally: "Fibrin ferment is present in the free state not only in circulating blood in small quantities, but also in small quantities is widely distributed throughout the entire organism." He finds by experiment that it is less active in circulating blood than in freshly shed blood, and determines the cause to be a rapid chemical change which takes place in the ferment immediately after the blood is shed. He calls the more active form *Thrombin* and the less active form in circulation *Prothrombin*. Further, he and others find that it is a *nucleoalbumin* derived from the katabolism of the nucleus. As to *Fibrinogen:* he has also found that widely disseminated, and has traced it back as a derivative from *Paraglobulin;* this in turn is derived from *Preglobulin,* and this from *cytoglobulin,* which is a derivative of cell protoplasm, or *cytoplasm.* The relation of these products to cell protoplasm on the one hand, and to coagulation on the other, is shown in the following diagram:

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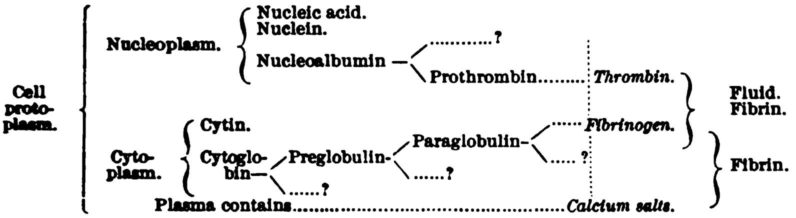
[1] The alkaline earths are Ca, Sr, and Ba. The blood contains calcium phosphate.



Pekelharing's theory must be mentioned here. Briefly stated it is as follows: *Thrombin differs from nucleoalbumin in its richness in calcium salts. Fibrin contains much calcium. Fibrin is probably a calcium compound of fibrinogen. In coagulation the calcium salt is probably dissociated from fibrin ferment and associated with fibrinogen, precipitating the latter in fine threads.* The difficulty with this theory is that it seems either to necessitate a quantitative relation between the amount of fibrin ferment and the amount of fibrin precipitated, or to make the thrombin a carrier of the calcium, in which case we would have to answer some puzzling questions as to where and how the changes occur. But the investigators in this field uniformly give the quantity of ferment as minute, and ascribe to it a real ferment action so that the small amount suffices to produce a considerable effect if the time be sufficient; furthermore, the calcium salts present in the plasma would seem to satisfy the conditions. All things considered the later theory of Schmidt and Hammarsten is as satisfactory as any.

VII. THE EFFECT OF HEMORRHAGE.

Repeated experiment has shown that one-fourth or one-third of the blood may be drawn without causing serious symptoms, and about one-half without causing death. One-half the circulating blood is supposed to be practically the limit. Whether the withdrawal of blood shall be more or less dangerous to life depends upon several complicating factors:

(*a*) **The Time** consumed in the withdrawal of the blood is an important factor. The experiments of Prevost and Dumas in 1823, and more recently those of Nasse, Vierordt and others, have shown that during a slow withdrawal the blood will be replenished from the lymph and plasma of the tissues, and if the hemorrhage cover sufficient time much more than 5 per cent. of the body weight may be withdrawn—*e. g.*, Tolmatscheff in seventy-one days drew from a dog blood equal in weight to 15 per cent. of the body weight. It is clear that in this case the withdrawal was sufficiently slow to enable the corpuscle-making organs to actually replenish the corpuscular elements. In this way may be demonstrated the rate at which the blood may be replenished. When the hemorrhage takes place within a shorter period—as one hour—the plasma alone will be in part replenished so that the blood last drawn would be much poorer in corpuscles than the blood first drawn.

(*b*) **The Circumstances** under which the hemorrhage takes place enters as a factor into the effect. For example, loss of a given quantity of blood from an animal under anæsthesia causes less disturbance of the system than the loss of the same quantity as a result of an accident. In the latter case ***shock*** enters in as a strong factor; in fact, it is much the stronger factor of the two.

VIII. TRANSFUSION.

1. **The Transfusion of Blood.**—The first recorded transfusion of blood was attempted by Lower in 1665. He successfully made a direct transfusion of blood from one dog to another directly after the latter had been bled to the death limit. The measure of the success of the transfusion is the fact that the second dog lived and showed no serious sequelæ of the operation.

In 1667 Denis successfully transfused the blood of a lamb to the circulatory system of a man. Subsequent attempts gave such a large percentage of failure that it fell quite into disrepute in the medical profession until after a long series of experiments upon lower animals. These experiments—for the most part performed during this century and many of them recently—have demonstrated the following facts: (I) The blood of the same species, or even of the same genus, may be *directly* transfused, but the danger of coagulation is very great. (II) The defibrinated blood of the same species or genus may be transfused (indirect transfusion), but the danger here rests in the introduction of a fluid which contains a very much larger percentage of thrombin than exists in normal blood; this excess of thrombin induces coagulation on the slightest provocation. The process of defibrination subjects the blood to the danger of introduction of particles of foreign matter—even bacteria.

All of these make the dangers of the transfusion of defibrinated blood too hazardous to be recognized by the medical profession as a solution of the question.

2. **The Transfusion of an Artificial Serum.**—It has been found that the most serious symptoms of rapid hemorrhage arise from ***sudden***

decrease of the amount of circulating fluid, together with a moderate *fall of blood pressure;* thus the principal indication to fulfil is *to replenish the quantity* of *fluid* without reference to the corpuscles or to the nutritive elements of the plasma. The fluid introduced must be of such a character as to cause no disturbance of the system. Warm, sterilized normal salt solution (NaCl 0.9 per cent.), injected either subcutaneously or into an exposed vein, has been successfully used in surgical and obstetric cases.

3. **Indications for Transfusion.**—(I) Dangerous hemorrhage or CO poisoning indicates injection of the above fluid. (II) Hæmophilia, the immediate indirect transfusion of blood of the same species. If the collapse is not too far advanced revival is possible.

2. THE LYMPH.

I. THE PHYSICAL PROPERTIES.

Like blood this liquid is composed of a plasma in which corpuscles float. The lymph plasma is quite like blood plasma in its composition and in its power to coagulate.

1. **Color.**—The lymph of the smaller lymphatics has a light yellowish color; that of the thoracic duct is yellowish opalescent or even milky. It assumes the latter color after a meal when it is laden with fat. In that condition it is usually called chyle.

2. **The Specific Gravity** of the lymph is 1012 to 1022.

3. **Amount.**—The amount of lymph has been estimated to be about two or three times the amount of the blood. The normal amount of chyle has been measured as between 3 or 4 kilos formed in twenty-four hours.

II. THE MORPHOLOGY OF THE LYMPH.

The structural elements of the lymph are the *leukocytes.* (Quid vide.)

III. THE CHEMICAL PROPERTIES OF THE LYMPH.

CONSTITUENTS.	LYMPH OF MAN.	CHYLE OF DOG.
WATER	94.2	90.67
SOLIDS	4.8	9.83
Organic	8.95	8.54
Proteids (serum albumin, serum globulin, fibrin)	3.75	2.21
Fats, lecithin, and cholesterin	0.10	6.10
Extractives (dextrose, urea, etc.)	0.10	0.23
Inorganic	0.85	0.79
Sodium chloride	0.56	
Sodium carbonate	0.24	
Other salts containing K, Ca, and traces of Mg and Fe as chlorides, sulphates, or phosphates	0.05	

Extractives containing dextrin, urea, kreatin, purin bodies, etc., are found in traces the same as in the blood, this being the origin of the same in the blood.

C. THE FORMATION AND DESTRUCTION OF THE CORPUSCLES.

1. THE ORIGIN OF THE RED BLOOD CORPUSCLES.

1. **During Intrauterine Life.**—The prenatal origin of the corpuscles may be subdivided into two periods, *the embryonic period* and *the fetal period.*

(*a*) **The Emtryonic Period** is characterized by the formation of blood and bloodvessels in the *vascular area* of the egg and of bloodvessels within the embryo. In both cases the fundaments of the circulatory system are formed from mesenchyme cells. Regarding the primitive red blood corpuscles we should remember that they "exhibit amœboid movements, have less than the usual quantity of hæmoglobin, are nucleated, globular, larger and more irregular and variable than the permanent corpuscles." Next they become normally colored, but they retain the nucleus during intrauterine life. They are capable of multiplication by karyokinesis. The relative number of non-nucleated corpuscles rapidly increase during the fetal period, in mammals, until at birth no nucleated corpuscle remain.

(*b*) **The Fetal Period.** After the establishment of the different systems of organs the formation of blood corpuscles goes on within the embryo. Neumann and Löwit observed the formation of nucleated blood corpuscles in the fetal *liver* and in the *spleen;* while Foa and Saviola observed it in the lymphatic glands.

2. **During Extrauterine Life.**—"The balance of evidence points to the formation of red blood corpuscles in extrauterine life—in all higher vertebrates—by the same process as in fetal life—*i. e.*, by karyokinesis of a typical cellular element—the erythroblast—which during extrauterine life is chiefly found in the red marrow of bones." (Bizzozero, Neumann.) The transition from the fetal method to the extrauterine method is not a sudden one, and the fetal method may be later employed after severe hemorrhages.

2. THE DECAY OF THE RED BLOOD CORPUSCLES.

Investigation has revealed the following facts: (I) There are fewer red blood corpuscles in the hepatic vein than in the portal vein. (II) The bile pigments are formed from hæmoglobin. (III) Disintegrated red blood corpuscles are to be seen in the cells of the spleen pulp. The conclusions to be drawn from these facts are: (I) The corpuscles in question meet their end in the *liver* and *spleen*. (II) At least a part of the hæmoglobin is lost in the excretion of the bile pigments. Further investigation shows that a part of the disintegrated corpuscles is taken up by the leukocytes and carried to the red marrow of bones—possibly to the spleen, and, in the former location at least, utilized by the erythroblasts in building up new corpuscles. It is estimated that the life of a red blood corpuscle is about three or four weeks.

3. THE FORMATION AND DESTRUCTION OF LEUKOCYTES.

The leukocytes are formed chiefly as lymph corpuscles in the lymphatic glands. The fine-meshed adenoid tissue of these glands seems to catch and hold all of the senile leukocytes and to allow only the more active corpuscles to pass through. Although many leukocytes are stopped by the lymphatic glands, there are very many more in the efferent than in the afferent stream. The necessary inference is that the lymph gland forms these new leukocytes and they enter the lymph stream and so pass into the circulation.

What has been observed in the relation of the lymphatic glands holds for the spleen, one of whose functions seems to be to detain the leukocytes which have engulfed senile red blood corpuscles. In some way the broken-down red blood corpuscle is transferred to the liver, probably through the agency of the leukocytes. The splenic vein contains far more leukocytes than the splenic artery. The spleen must be a nidus for their formation.

The leukocytes are destroyed in the blood and lymph by simple disintegration, giving origin, at least in part, to the prothrombin mentioned under coagulation.

4. SUMMARY OF THE FUNCTIONS OF THE SPLEEN.

The spleen is as completely and exclusively connected with the circulatory system as is the heart. The general function of the spleen seems to be to keep the corpuscular elements of the blood constant, or at least to assist in that important office.

The specific functions of the spleen are obscure. Some idea of its functions may be gained by the following methods:

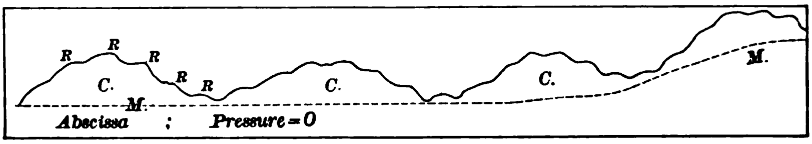
(*a*) **By Extirpation.**—The removal of a dog's spleen seems to make no essential difference in his general physical condition. After a few weeks an enlargement of the lymph glands and an increase of the red marrow of the long bones occur.

(*b*) **By Chemical Examination** it is found, 1st, that the spleen yields a preponderance of those inorganic salts found in the red blood corpuscles; 2d, that the extractives are such as are produced by the breaking up of proteids.

(*c*) **By Microscopic Examination after Hemorrhage.**—The spleen normally contains large leukocytes which have taken in one or more red blood corpuscles, but after hemorrhage also numerous red nucleated hematoblasts (homologues to the erythroblasts of red marrow of bones).

(*d*) **By Oncometer Curves.** (See Fig. 91.)—An oncometer is a metallic case made for the purpose of enclosing an active organ. The space between the organ and the case is filled with warm saline solution. Any change in the volume of the organ affects the recording apparatus by transmission through a column of liquid which is continuous with that which surrounds the organ.

FIG. 91



R R, respiratory waves; *C C C*, waves of rhythmic contraction of muscle tissue of capsule and trabeculæ; *M M*, wave occurring four to five hours after a meal. Waves *R R* evidently depend upon general blood pressure. Heart waves do not show in the oncometer curve. The waves *C C* probably show an independent action of the spleen directed to the partial emptying out of its blood. The wave *M* is probably caused by a heaping up of absorbed foodstuffs.

D. THE CIRCULATION OF THE FLUIDS.

The best general idea of the course which the blood takes in its circuit through the body may be gotten from such a schema as that shown in the accompanying figure (Fig. 92).

1. THE ACTION OF THE HEART.

In order to observe directly the movements of the heart one may institute artificial respiration, open the chest, tying all bleeding vessels, open the pericardium, and note at leisure the movements of the organ while it works under the slightly changed conditions.

In such an experiment one may observe: (I) A series of contractions (systole) alternating with a series of dilatations (diastole). (II) Auricular contraction preceding ventricular contraction. (III) Auricular contraction beginning with the contraction of the muscle fibres which encircle the large veins, immediately thereupon involving the whole auricular wall. (IV) The auricles contracting simultaneously, but not completely emptied when the ventricular contraction begins. (V) Auricular systole ends at the moment that ventricular systole begins. (VI) The ventricles begin their contraction simultaneously and cease simultaneously.

FIG. 92

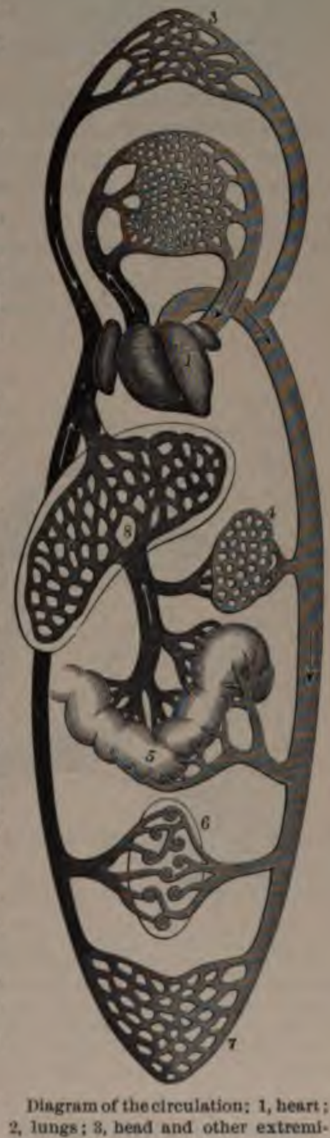


Diagram of the circulation: 1, heart; 2, lungs; 3, head and other extremities; 4, spleen; 5, intestine; 6, kidney; 7, lower extremities; 8, liver. (Dalton.)

a. Changes of Form which the Heart Undergoes.

(*a*) **Observed in the Open Thorax** of a mammal, which is lying upon its back.

(*α*) DURING DIASTOLE the transverse diameter becomes markedly greater and the dorsoventral diameter less than in systole giving an elliptic outline.

While filling, all of its dimensions increase, though the lateral diameter increases somewhat more than the dorsoventral, owing to the bulging of the flaccid right ventricular wall on the right side.

(*β*) DURING SYSTOLE the transverse diameter becomes shorter and the dorsoventral longer, approaching a circle in outline. The three factors which work together to produce this change are: (I) The intraventricular change of pressure; (II) the force of gravitation; (III) the atmospheric pressure.

(*b*) **Observed in the Closed Thorax** of a mammal by the use of needles passed through the thoracic wall into the heart wall at different angles and location. For the following facts we are indebted to Haycraft:

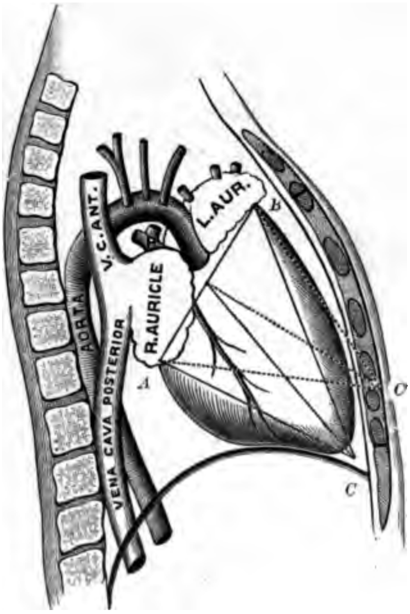
(*α*) DURING DIASTOLE the heart hangs passive in its pericardium, suspended by its connection with the great vessels which enter or leave its base.

(*β*) DURING SYSTOLE all of the dimensions of the heart decrease, but any increase of lateral over dorsoventral dimension is compensated during systole, so that the cross-section of the heart at the end of systole presents nearly a circular outline. The *anteroposterior dimensions*, or the distance between base and apex, also decrease, but the apex is not in consequence drawn away from the chest wall. The reason for this will be discussed under the next topic.

b. Changes of Position of the Heart Incident to its Activity.

1. Mechanical Factors which Tend to Produce a Change in the Position of the Heart.—These factors may be enumerated as follows: (*α*) *The Asymmetric Position* which the apex takes during diastole because of the action of gravity. (*β*) The condition of *pressure equilibrium* and *tension equilibrium* of closed cavities. Whenever the pressure increases within a liquid-filled sac, the latter *tends to erect* and stand in such a position that the tension on each part of the wall shall be equal. (*γ*) *The Recoil.* Whenever a closed receptacle ejects its contents through action of a force mechanically within itself, the structure *undergoes a recoil* in obedience to Newton's law of motion that "action and reaction are equal and in opposite directions." (*δ*) *The base of the heart is relatively firmly fixed;* the vertebral column forming the basis of fixation, the large vessels being held well in place by strong connective-tissue attachments. Besides this the arch of the aorta passes over the root of the left lung, while the pulmonary artery passes directly into the root of both lungs.

FIG. 93



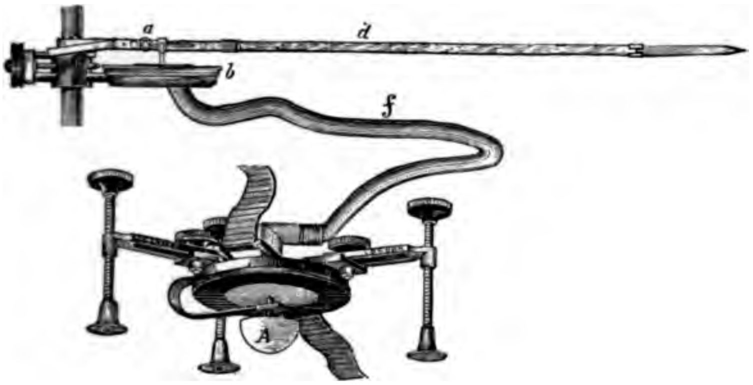
A diagram showing Ludwig's theory of the erection of the ventricle during systole. The base of the heart, *A B*, is rather firmly fixed. In diastole the apex takes the position, *A B C*, as outlined in the figure. In systole it tends to erect by intraventricular pressure and stand in the position *A B C'*.

2. The Influence of the Enumerated Factors upon the Action of the Heart.—(*a*) **The Sudden Rise of Intraventricular Pressure during Auricular Systole** would have two tendencies: (I) To cause the apex to assume a more symmetric position with respect to the base—*i. e.*, to give the apex an impulse against the chest wall; (II) the light auricles would tend to recoil strongly, but this would be largely counteracted by tissues above the auricles, as well as by the weight of the columns of blood in the vena cava anterior and the pulmonary veins.

(*b*) **The Great Rise in Intraventricular Pressure during Ventricular Systole** gives the apex a sudden and strong impulse toward the point of symmetry—*i. e.*, toward the thoracic wall just at the beginning of ventricular systole. (See Fig. 93.) After the position of symmetry has been assumed there will be a tendency for either a sustained crest or for a gradual fall, the latter owing to a decrease in the dimensions of the ventricle and not to a falling from the position of symmetry.

(*c*) **There will be a Recoil of the Heart** when the contents of the ventricular cavity are ejected into the arteries; but the direction of recoil is at nearly right angles with the direction of the movement of the apex when coming into the position of symmetry—*i. e.*, the direction of recoil is in the line determined approximately by the axis of the left ventricle.

FIG. 94

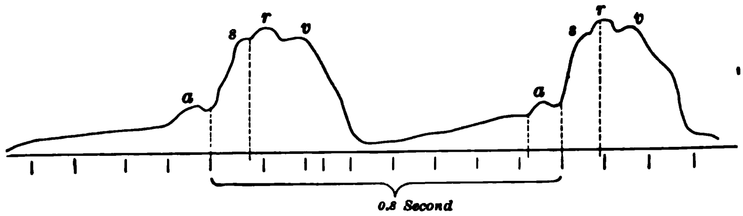


The cardiograph. (Chapman.)

(*d*) **Observation of the Heart** in the closed thorax may be made with a *cardiograph*. This instrument, shown in Fig. 94, consists of a pair of Marey tambours. The receiving tambour is provided with a button, *A*, which is placed over the site of the apex beat of the heart. Movements of the button affect directly the membrane of the receiving tambour. Through the connecting tube, *f*, movements of the receiving tambour are transmitted to the recording tambour, *b*, whose membrane supports the recording lever, *d*. The tracing point of this lever may be brought into contact with a kymograph drum and a permanent and exact record made of the movements of the thoracic wall produced by the apex beat of the heart.

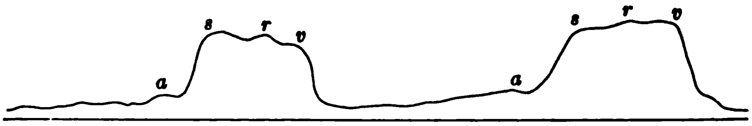
From what has been said regarding the relative influence of the erection and the recoil of the ventricle, it is evident that the recoil will variously affect the cardiogram according to the position of the subject under observation. Furthermore, the force of the recoil will be broken by just that factor which emphasizes the action of heart in assuming a symmetric position, namely, the fixing of the base of the heart. The recoil affects the cardiogram in different ways, if it appears at all. If there is only one superimposed wave beyond the systolic rise, that one wave may be taken to represent the effect of the closure of the semilunar valves, unless it is within 0.1 of a *second from* the *beginning* of the *systolic wave.* Any wave between the systolic wave crest and the semilunar wave may be

FIG. 95



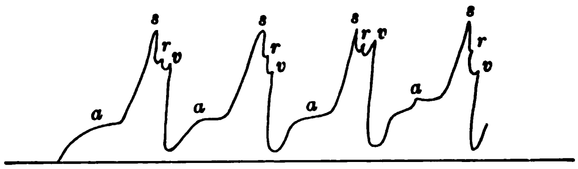
Cardiogram taken by Chauveau and Marey: *a*, auricle wave; *s*, systolic rise; *r*, recoil wave; *v*, valvular wave.

FIG. 96



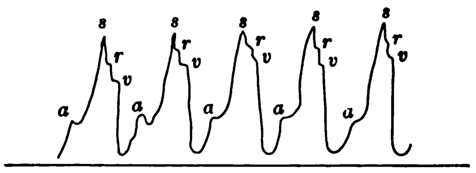
Cardiogram taken by Edgren.

FIG. 97



Cardiogram taken by Sanderson, with fast drum.

FIG. 98



Cardiogram taken at the Physiologic Laboratory of the Northwestern University Medical School.

taken as the recoil wave. Especially strong is the evidence favoring that interpretation, provided the wave in question falls between 0.05 second and 0.1 second after the beginning of the systolic wave. Should the cardiogram present other small superimposed crests they may be interpreted as *instrumental—i. e.*, formed by secondary vibrations of the membranes or of the elastic media of transmission. (See Figs. 95, 96, 97, 98.)

c. Changes of Pressure within the Heart Incident to its Activities: Intraventricular Pressure.

The strong contractions of the muscle tissue of the walls of the heart *cause* the cavity of the ventricle to be decreased in volume during systole; while the relaxation *permits* the increase of the volume of the ventricular cavity during diastole. This cavity is constantly filled with blood. At the beginning of systole there are about 180 c.c. of blood in each ventricle; at the end of systole the ventricles are practically empty. The contraction of the ventricles subjects the liquid contents to sufficient pressure to eject it into the aorta and pulmonary artery. Liquids flow from a point of higher pressure to a point of lower pressure. The pressure in the arteries named must be sufficient to overcome all resistance beyond, otherwise the blood could not flow out of them through the capillaries and into the veins. The pressure in the ventricles, in turn, must be higher than the pressure in the large arteries, otherwise the blood could not flow from the ventricles into the arteries. The pressure necessary to force the blood out of the ventricles is produced by the contraction of the ventricular walls upon the ventricular contents. The ventricle is, then, a *force pump.*

The ancients, from Aristotle to and including Galen, believed the heart to be a *suction pump.* They thought that the ventricles actively dilated, drawing the blood in; then actively contracted, forcing it out. Harvey showed that the dilatation of the ventricles is passive, and that only the contraction is active.

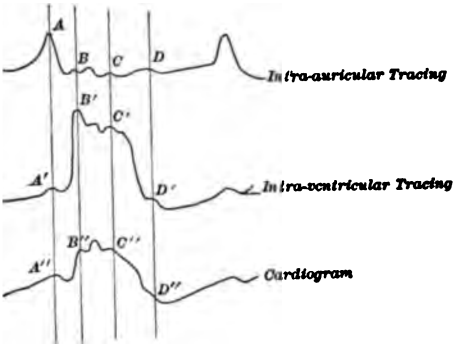
The question of intraventricular pressure has been a much debated one for a long period.

Physiologists have endeavored to determine not only the range of variation of pressure within the ventricles, but also the variations of pressure which occur between the maximum and the minimum; in other words, to determine the qualitative as well as the quantitative changes of pressure.

Three different devices have been contrived for this purpose. Chauveau and Marey used a modification of the Marey tambours. The recording tambour having the usual construction but the receiving tambour was a small, inflated, rubber bulb. A double-lumened tube, bearing one bulb at its end connected with one lumen, and another bulb a few centimetres above the end connected with the other lumen, was joined to two recording tambours, one communicating with each bulb. The tube was introduced, through the jugular vein, into the right side of the heart. The bulbs were so located that the end bulb passed into the cavity of the right ventricle while the other one reached to the auricular cavity. A third pair of tambours was arranged to record the movements of the apex of the heart. In this way three synchronous tracings were recorded: (I) variations of the *intra-auricular pressure*, (II) variations of the *intraventricular pressure*, and (III) a *cardiogram*. (See Fig. 99.)

These tracings make it evident: (I) that auricular pressure reaches a maximum before ventricular pressure begins; (II) that during high ventricular pressure the auricular pressure is at a minimum. This method, however, gives only qualitative changes, and is subject to errors in its elastic transmission.

FIG. 99



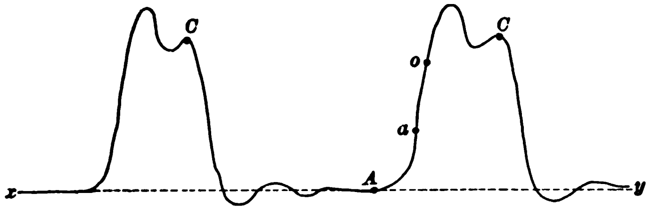
Intracardiac pressure tracings obtained by Chauveau and Marey. The vertical lines show the synchronous parts of the tracings. A, A', A'', effect of auricular systole; B, B', B'', effect of ventricular systole; C, C', C'', effect of closure of ventricular systole.

In 1878 Goltz and Gaule ("Ueber die Saugkraft des Herzens," *Archiv. f. d. ges. Physiol.*, Bd. xvii., S. 100) used a new technique. They devised a mercury manometer provided with a reversible valve. Turned in one direction the manometer records only maximum pressures; reversed, it records only minimum pressures. This manometer was put into communication with the ventricular cavities through an inelastic connecting tube introduced along a bloodvessel into the cavity to be tested. This method showed a maximum (left) *intraventricular* pressure of 176 to 234 mm. of mercury; a minimum pressure of —30 mm. to —38 mm. of mercury. In the right ventricle the maximum was 26 to 72 mm.; the minimum was —8 to —25 mm. In every experiment the maximum pressure in the left ventricle was 18 to 22 mm. greater than the maximum aortic pressure. Note that the minimum pressure is less than atmospheric pressure. That seems to justify the conclusion that the ventricle exerts a suction equal to 30 to 38 mm. of mercury. In this connection we must not forget that the heart is enclosed in a sealed cavity whose pressure is usually negative, though this negative pressure is greater during inspiration than during expiration. If a minimum manometer be introduced into the thorax the mercury will fall from 9 to 40 mm. according to the character of the respiration, 9 in quiet inspiration and 30 to 40 in forced inspiration. In any particular observation the manometer registers the lowest pressure reached in any inspiration made by the animal during the observation. If the manometer tube be passed on into the ventricle it will register the lowest pressure reached in any diastole during the experiment.

If the *intraventricular* is no lower than the intrathoracic pressure there could be no suction of the blood from the thoracic vessels or auricles into the heart. The figures given above for intraventricular pressure and intrathoracic pressure indicate that there may or may not be a slight suction upon the thoracic blood. In quiet breathing one would expect the negative pressure of the ventricle to exceed that of the thorax by about 20 mm. of mercury.

In 1894 Gaule said, regarding his results: "At the beginning of diastole any occurrence of negative intraventricular pressure is to be attributed to the sudden widening of the base of the aorta on the closure of the semilunar valves, thus suddenly opening the upper end of the ventricular cavity."

FIG. 100



Curve from left ventricle: *x y*, zero line, or atmospheric pressure; *A*, part of curve due to intra-auricular pressure; *a*, auriculoventricular valves closed; *o*, semilunar valves open; *C*, semilunar valves closed; *C A*, period of ventricular diastole. (Rolleston.)

A third method of recording the variations of intraventricular pressure has been elaborated by Rolleston. His instrument consists of a delicate brass cylinder with hard rubber piston. The piston receives the pressure of the atmosphere upon one side and that of the blood upon the other—the blood-pressure being transmitted to the cylinder through a long trocar introduced into the ventricular cavity. The piston in turn moves a writing lever whose rise and fall is controlled by the resistance to torsion of a steel ribbon. This apparatus has the great advantage of showing not only qualitative but quantitative changes of pressure, for the value of the steel spring may be determined in advance. "Rolleston's conclusions are as follows: (I) There is no distinct and separate auricular contraction marked in the curves obtained from either right or left ventricles, the auricular and ventricular increase of pressure being merged into one continuous rise. (II) The auriculoventricular valves are closed before any rise of pressure within the ventricle above that which results from the auricular systole. (III) The semilunar valves open at the point situated about the junction of the middle and upper thirds of the ascending limb of the curve (*o*) and the closure about the beginning of the descending limb (*c*). (IV) Regarding the *minimum pressure* Rolleston's conclusion is: "The minimum pressure in the ventricle MAY fall below that of the atmosphere, but the amount varies considerably." (See Fig. 100.)

SUMMARY.

(*a*) **The Work of the Auricle** is accomplished in its systole, which drives into the ventricle the blood which it has received from the veins. The thin-walled auricle, in common with the thin-walled veins, expands, under the negative intrathoracic pressure, to receive the venous blood which rushes into the thorax during inspiration. The structure of the auricles is such that the pressure within them can never fall below that of the thorax in general.

(*b*) **The Work of the Ventricle** is accomplished in its systole, which drives into the arteries the blood which it has received from the auricle.

(*c*) **The Walls of the Ventricle** will be passively dilated by the negative intrathoracic pressure, but the negative pressure within the ventricle could, by this cause, never exceed the negative pressure of the thorax. But the negative pressure of the ventricle frequently does exceed the negative pressure of the cavity which contains it. There are two ways to account for this:

(α) The natural position of absolute relaxation does not completely close the ventricular cavity. The active contraction of systole carries the walls beyond this position of absolute relaxation in order to completely empty the ventricle. At the end of systole the walls spring back by their natural elasticity to the position of absolute relaxation, thus exerting a momentary negative pressure beyond that of the surrounding thorax.

(β) The sudden expansion of the upper part of the ventricle by the widening aorta, as suggested by Gaule, has been mentioned above. But in these changes the muscular tissue of the ventricle is absolutely passive.

Events of the Cardiac Cycle.—Tabulated.

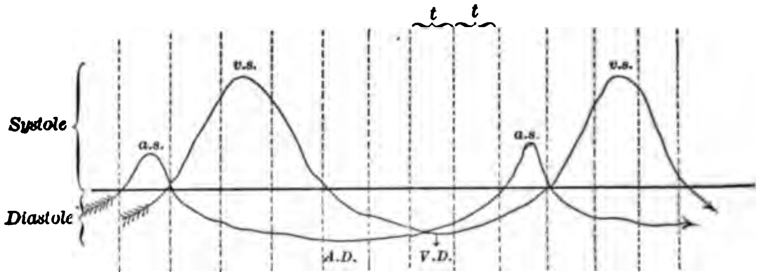
The Cardiac Cycle.

Event.	Condition of		Force Involved.	Direction of Blood Current.				Condition of	
	Ventricle at Beginning.	Auricle at Beginning.		Ways Possible.		Ways Determined.		Auricle at End.	Ventricle at End.
				I. and II.		I.	II.		
1. Auricular systole	Filling.	Full	Contraction of auricular walls.	To ventricle.	To veins.	**Open** to ventricle by relaxation of walls and opening of valves.	**Blocked** to veins by counterpressure and contraction of veins.	Empty.	Full.
2. Ventricular systole.	Full.	Empty or filling.	Contraction of ventricular walls.	To arteries.	To auricle.	**Open** to arteries by lower pressure and opening valves.	**Blocked** to auricle by the auriculoventricular valves.	Filling.	Empty.
3. Rest or diastole.	Empty.	Filling.	Aspiration of thorax, elasticity of lungs, muscular contractions, etc.			**Open** to auricle by lower pressure.	**Open** to ventricle by lower pressure and open valve.	Full.	Filling.

d. The Cardiac Cycle.

The term *cardiac cycle* has been applied to the ever-recurring series of events which are repeated about once every second in the human heart. Briefly rehearsed, these events are: (I) *The auricular systole,* which empties the auricle and fills the ventricle, and which ends with the closure of the auriculoventricular valves. (II) *The ventricular systole,* which empties the ventricle into the artery through the forced semilunar valves. During the ventricular systole the auricle is filling. (III) *Rest,* which includes all of the ventricular diastole and a little more than half of the auricular diastole. During the *rest period* blood is flowing freely into the auricle and through the auriculoventricular valve into the ventricle.

FIG. 101



Time relations of heart cycle: *t*, 0.1 second of time; *a.s.*, auricular systole, 0.1 sec.; *v.s.*, ventricular systole, 0.3 sec.; *V.D.*, ventricular diastole, 0.5 sec.; *A.D.*, auricular diastole, 0.7 sec. Total cardiac cycle, 0.8 sec.

The time of the average heart cycle in the human male adult is 0.8 second, which is distributed as follows:

The ventricular systole consumes 0.3 second; diastole, 0.5 second. The auricular systole consumes 0.1 second and the diastole 0.7 second. Heart systole, 0.4 second; heart diastole, 0.4 second. (See Fig. 101.)

e. The Work Done by the Heart.

1. **Data.**—(I) Maximum pressure in left ventricle varies between 140 to 200 mm. Hg. (II) The maximum pressure in right ventricle is about 60 mm. Hg. (III) The amount of blood ejected against the above pressure varies, for the left (or right) ventricle from 120 to 180 c.c.

2. **To Derive a Special Formula for Work of Heart.**

Formula: Let W = work done.
" h = height in centimetres.
" g = weight in grams.
" m = centimetres of Hg pressure.
" b = number of c.c. of blood ejected at one systole.

A general formula for work done when the work is to be expressed in Gm.-cm. is: $W = g \times h$. To determine W, we have first to find the value of g and h. A pressure of m centimetres of mercury would be equal to a pressure of 13.6 m centimetres of water and $\frac{13.6\,m}{1.055}$ cm. of blood. The work done in ejecting from the heart g grams of blood against m centimetres of mercury pressure would be the same as the work done in raising g grams of blood to the height of $\frac{13.6\,m}{1.055}$ cm. What is the weight of b cubic centimetres of blood? Naturally the volume times the specific gravity; or $g = b \times 1.055$. The formula would therefore be:

$$W = \frac{b \times 1.055}{1} \times \frac{13.6 \times m}{1.055} \text{ or } W = 13.6\,bm.$$

3. **Problems.**—(*a*) **How Much Work** does the left ventricle perform in each systole if 120 c.c. of blood is ejected against 15 cm. of mercury pressure? $W = 13.6 \times 120 \times 15 = 24{,}480$ gram-centimetres.

(*b*) **How Much Work** does the heart perform at each systole if the right ventricle expels the same quantity of blood against two-fifths as great pressure? $W = 13.6 \times 120 \times 14 \times \frac{7}{5} = 34{,}272$ Gm.-cm. That is, both ventricles will do $\frac{7}{5}$ of the work done by left ventricle alone.

(*c*) **How Much Work** will the heart do in twenty-four hours if it ejects 150 c.c. of blood into the arteries against 150 mm. of Hg pressure at the rate of sixty beats per minute. $W = 13.6 \times 15 \times 150 \times 60 \times 60 \times 24 \times \frac{7}{5} = 3{,}701{,}376{,}000$ Gm.-cm.

(*d*) **How Many Metres** would that amount of work lift the body of a man of 60 Ko. weight?

$$W = \frac{13.6 \times 15 \times 150 \times 60 \times 60 \times 24}{1000 \times 100 \times 60} \times \frac{7}{5} = 616.9 \text{ metres.}$$

It would take about three hours of hard climbing for a man to lift his body through 616.9 metres; so that the heart can do about one-half as much work as all of those skeletal muscles involved in locomotion or, in fact, in manual labor.

I. The Sounds of the Heart.

1. **Character.**—There is a succession of two sounds separated by a pulse—lŭb-dŭp—lŭb-dŭp, etc. The first sound (lŭb) is longer in duration and lower in pitch than the second.

2. **Cause of the Heart Sounds.** (*a*) **The First Sound.**—It is synchronous with ventricular systole; it is, therefore, universally associated with the events which are taking place in the heart at the time: (I) vigorous muscular contractions; (II) friction of blood

rushing through the semilunar valves; (III) friction of surface of heart incident to its change of shape within the pericardium; (IV) friction of heart against neighboring structures in the thorax incident to its change of position in the thorax. As any one of these four factors may be variously modified by various diseases, it is evident that a close study of the normal heart sounds is of great importance.

(*b*) **The Second Sound** of the heart is synchronous with the closure of the semilunar valves of the aorta and pulmonary artery, and as the quality of the sound is such as might readily be attributed to the closure of those valves, it is generally interpreted in that way. The fact that a lesion of these valves makes a marked change in the quality of the second sound would seem to demonstrate conclusively that the closure of the semilunar valves is at least the most important factor in the second sound.

The most advantageous position for hearing the first sound is at the apex, while the second sound is most easily heard over the base of the heart.

2. THE CIRCULATION OF THE BLOOD.

The problems of this field of physiology are physical problems, of the flow of liquids through tubes. As far as arterial circulation is concerned the phenomena are those *of the flow of liquids through elastic tubes under the influence of an intermittent initial force.* For the physical presentation of these problems see the physical introduction to this chapter.

a. The Circulation in the Arteries.

1. **Cause.**—There is one, and only one, cause for the flow of blood in the arteries, namely, *ventricular systole.* The high intraventricular pressure induced by the systolic contraction is transmitted to the large arterial trunks. The blood flows from the left ventricle to the aorta because the pressure is higher in the ventricle than in the aorta; it flows from the aorta into its branches because the pressure is higher in the aorta than in its branches, and so on, the energy of ventricular systole being gradually expended in overcoming resistance, so that the lateral pressure gradually decreases from the ventricle to the capillaries.

The initial energy is, however, not all expended in forcing the blood to and through the capillaries, so that there is still a small residuum of heart energy left when the blood enters the veins to assist other factors in returning the blood to the heart.

2. **Blood Pressure.** (*a*) **Methods of Determining.**—The blood-pressure is usually determined by the use either of a mercurial manometer or of a spring manometer. The mercurial manometer

was first used and modified for this purpose by Ludwig. His complete apparatus for measuring and recording the quantity and variations of blood pressure consists of the mercurial manometer whose proximal limb is connected to the artery through a lead or rubber tube and cannula filled with a solution which will retard the coagulation of the blood. The distal limb is fitted with an ivory float which bears a tracing point. The complete manometer as described is fixed to a recording apparatus which consists of a rotating cylinder propelled by clockwork. Originally the whole apparatus was called a *kymographion* (wave writer); later the term kymographion, shortened to kymograph, has been applied to the recording drum, which is now extensively used in experimental physiology.

A very valuable modification of the Ludwig apparatus has been suggested: A small tambour is joined to the distal end of the manometer by a piece of pressure tubing and supplied with a very delicate tracing lever which magnifies the movements of the membrane ten to twenty times, as desired, the levers being variable in the construction of the instrument. The surface of the tambour should not be larger than 15 mm. in diameter. With this ratio between the tambour surface and the mercury surface, and the levers multiplying ten to twenty times, a most beautiful arterial tracing can be obtained, showing not only the respiratory and percussion waves, but also the dicrotic wave clearly superimposed on each cardiac wave.

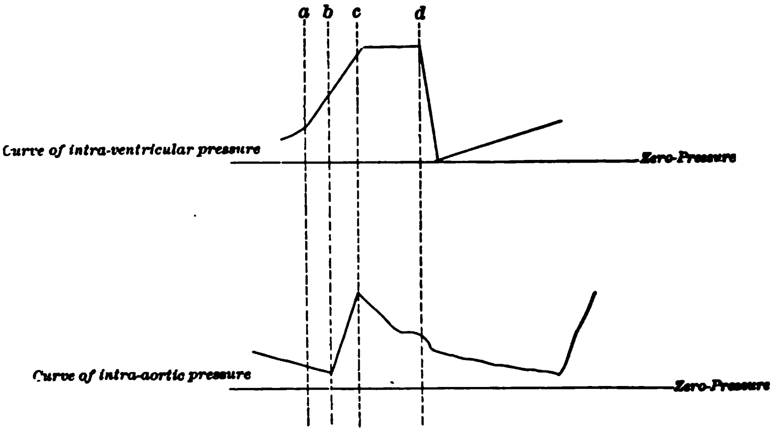
The spring manometer of Fick utilizes the principle that pressure of liquid within a tube tends to straighten the tube. A thin C-shaped steel tube is brought into connection with an artery. The pressure of the blood transmitted through the connections to the liquid within the C-tube will straighten it slightly. The proximal end of the tube being fixed, the distal end moves back and forth with each vibration of pressure.

The mercury manometer gives a very exact measure of the amount of the pressure within the artery, but the inertia of the float is too great to permit it to follow faithfully the minor variations of pressure. It shows the Traube-Hering curve, the respiratory wave, and the systolic wave, but it does not show the dicrotic wave. The manometer tambour, however, traces the dicrotic wave, but fails to show the Traube-Hering wave. The spring manometer also shows the dicrotic wave, but not the Traube-Hering wave.

(*b*) **Relation of Arterial Pressure to Intraventricular Pressure.**—As stated above, the arterial pressure is the transmitted, intraventricular pressure. The accompanying figure (Fig. 102) shows that pressure within the aorta does not rise until the opening of the semilunar valves; that the crest of the systolic wave of aortic pressure coincides near the heart, with the crest of the intraventricular (systolic) wave; that there is no "plateau" of pressure in the artery; that the closure of the semilunar valves marks the beginning of the fall in the ventricular wave and a superimposed (dicrotic) arterial wave; and that arterial pressure continues to fall until the semilunar valves open again.

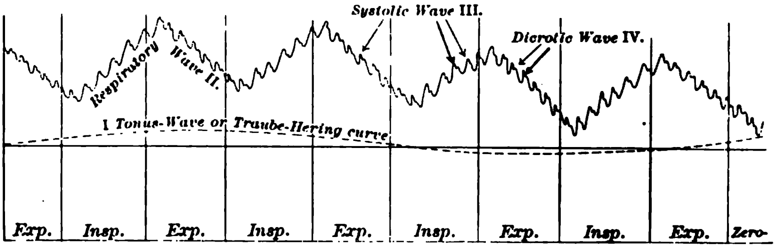
(c) **Variations of Arterial Pressure.**—(a) CYCLIC VARIATIONS may be considered as: (I) Cycle of variation due to *heart contraction*. (See Fig. 103, waves *III* and *IV*.) The rounded systolic wave, as shown by a mercurial manometer, or the systolic with its superimposed dicrotic wave, belongs to this class. (II) Cycle of variations due to the rhythmic action of the *respiratory* musculature. (Wave *II*.)

FIG. 102


a
b
c
d
Curve of intra-ventricular pressure
Zero-Pressure
Curve of intra-aortic pressure
Zero-Pressure

Showing the relation of arterial pressure to intraventricular pressure. Time relations: *a*, beginning of auricular systole; *b*, opening of semilunar systole; *c*, maximum of systolic pressure: *d*, closure of semilunar valves.

FIG. 103



A typical tracing of arterial blood pressure.

Respiratory wave *II* is the result of the influence of the respiratory musculature. How is this result brought about? Note: 1st, that the pressure rises during inspiration; 2d, that it falls during expiration; 3d, that the maximum pressure occurs after the end of the inspiratory movement; and 4th, that the minimum pressure occurs after the end of expiration. The pressure rises during inspiration because there is greater negative pressure in the thorax, drawing more venous blood to the right auricle and leading either to a greater quantity of blood being ejected from the heart at each systole, or to an increase of the rate of the heart beats. The pressure falls during expiration for reasons the converse of those just stated. The maximum pressure occurs after the end of inspiration and the minimum pressure after the end of expiration, because there is a lapse of about one second before the change wrought by respiratory movements can have its effect on the quantity of blood ejected from the *left ventricle.*

(3) PERIODIC VARIATION, due to changes in arterial tonus or to the degree of constriction under the influence of the vasomotor nerves. (See Fig. 103, wave *I.*) These long waves are called Traube-Hering curves because first discovered and described by the men whose names they bear.

(d) **Laws of Arterial Blood Pressure.**—(*a*) A GENERAL FORMULA which summarizes the laws of arterial blood pressure may be expressed mathematically: $P = Hr \times Hs \times R$, when P equals pressure; Hr, heart rate; Hs, heart strength; and R, peripheral resistance. This formula may be verbally expressed as follows:

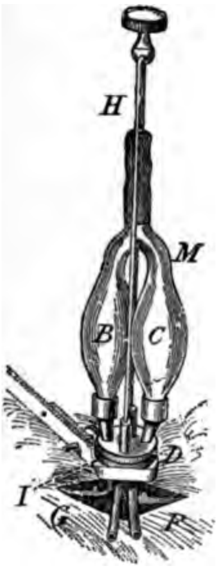
(b) LAWS OF ARTERIAL BLOOD PRESSURE: (I) *The pressure will vary with the rate of the heart,* when the strength of the systole and the peripheral resistance remain unchanged. (II) *The pressure will vary with the strength of heart systole,* when the rate and resistance remain unchanged. (III) *The pressure will vary with the peripheral resistance,* when the rate and strength of heart systole remain unchanged. (IV) *The pressure may remain unchanged if one or two of the factors increase while the remaining factor (or factors) decreases in value.* (V) *If all the factors increase at the same time a very great increase in pressure may result.* (VI) *If all the factors decrease at the same time the pressure will fall proportionately.* (VII) *The factors of blood pressure are under the control of the nervous system.*

3. **The Velocity of the Flow.** (*a*) **Methods of Determining.**—One of the earliest methods—that of Volkmann (1850)—consisted of a U-tube 25 cm. in length. The lumen of the tube is made continuous with the lumen of the artery by severing the latter and placing the proximal end over an entrance cannula and the distal end over an exit cannula. Two 3-way stopcocks control the entrance and exit. In the adjustment shown in the left-hand figure the blood passes directly through the instrument. When the cocks are turned as indicated in the right-hand figure the blood passes along the U-tube. In making an observation the tube was filled with water, which was driven into the artery when the tube filled. The time required for the stream to advance 25 cm. was taken to equal the velocity of flow in the artery of the same lumen. The results were far short of the actual velocity because of the resistance of the apparatus, and the

contraction of the distal end artery due to the action of the water upon it.

Ludwig's stromuhr is a modification of the principle used by Volkmann. The U-tube is replaced by a double chamber (Fig. 104) whose volume is known. Instead of stopcocks, the chambers opening through plate *D* communicate with the cannulæ which open through plate *I*. After one of the chambers is filled the plate *D* is quickly rotated through 180°, with the aid of the milled head above *H*. This reverses the direction of the stream through the chambers. The proximal chamber (*C*) is filled with oil, the distal chamber (*B*) with normal saline solution, through the tube *H*, which is thereupon clamped. The proximal cannula (*F*) is inserted into the proximal end of the cut artery. The plate *D* is turned just enough to shut off the continuity of the lumen. To make an observation, turn the plate *D* through 180°, taking the time to fifths of a second; the blood rushes through the proximal cannula up into chamber *C;* the oil floats upon the blood without mixing with it, and flows into chamber *B*, pushing the warmed saline solution into the distal portion of the artery. When the blood has reached the point at which the oil stood in the first adjustment the instrument is reversed, time noted, and the chamber *B* (now the oil-filled, proximal chamber) receives the blood from the proximal cannula (*F*), while the blood in chamber *C* is passed on into the artery.

FIG. 104



Ludwig's stromuhr.

With this instrument one determines in advance the *radius* (r) of the cannula, which is chosen for an artery of approximately equal radius; the *quantity* (q) which the chamber contains. During the experiment one observes the *time* (t) in seconds required to fill the chamber; n, *number* of times. The following formula may be used: *Velocity* (v) equals a constant factor $\left(\frac{q}{\pi r^2}\right)$ multiplied by the number of times the chamber filled (n) and divided by the time (t) required to fill it n times, or $v = \frac{qn}{\pi r^2 t}$.

Chauveau's dromograph consists of a brass tube to be inserted into the lumen of a severed artery. The blood flowing through the tube pressed against the lower end of a needle pivoted in the wall of the tube, deflecting it from its zero position by overcoming a resistance. The distal end of the needle indicated upon a dial the relative velocity of the stream within the tube.

(*b*) **Velocity as Determined** by the Ludwig stromuhr in the carotid artery of a dog varied between 34.9 cm. and 73.3 cm. per second during a total observation period of 80 seconds, in which time five readings were taken. The average for the five observations was 49 cm. per second through a carotid whose lumen was 2.7 mm. Similar observations on a rabbit yielded a velocity of 15.8 cm. per second through a carotid with a 1.4 mm. lumen.

The Chauveau dromograph reveals a difference of velocity during the different phases of the pulse wave: In the carotid artery of a horse the velocity reached 52 cm. per second during systole, dropped to 22 cm. per second at the time of the dicrotic wave, and to 15 cm. per second during diastole.

(*c*) **Variation of Velocity.** (*α*) DEPENDENT UPON CROSS-SECTIONAL AREA.—The discharge of any stream through a channel or system of channels equals the mean velocity multiplied by the cross-sectional area at the point of observation ($D = v \times a$). Therefore, the velocity equals the discharge divided by the sectional area $\left(v = \frac{D}{a}\right)$. If the discharge remains constant the velocity will vary inversely as the sectional area $\left(v \propto \frac{1}{a}\right)$. The total sectional area of the primary branches from the aorta is several times as great as the area of the aorta between the heart and the arch; the mean velocity in these primary branches is, therefore, as many times smaller than the initial velocity, as their combined area is greater than that of the base of the aorta.

Volkmann determined the average velocity of the capillaries to be approximately $\frac{1}{500}$ as great as the velocity in the aorta. We may reason backward and conclude that the combined sectional area of all the capillaries equals approximately 500 times the sectional area of the aorta at the base. The vasomotor muscle-nerve system may induce variation of terminal sectional area, and therefore influence velocity in the periphery. As the blood returns toward the heart the total sectional area of the veins at different distances from the heart becomes progressively smaller and smaller, thus causing the current to flow faster and faster until it reaches the heart. The combined area of the two venæ cavæ being about twice that of the aorta, the blood enters the right auricle with a velocity about one-half that of the flow in the aorta.

(*β*) VELOCITY DEPENDENT UPON FACTORS OF BLOOD PRESSURE.—The factors of blood pressure are rate and strength of heart action, and peripheral resistance ($P = Hr \times Hs \times R$). If the general peripheral resistance be much increased while the heart action remains unchanged the pressure will be much increased, but the velocity will be decreased because of the difficulty of exit from the arteries through the arterioles and capillaries.

The relation between the velocity and the heart action is direct; while that between velocity and peripheral resistance is reciprocal $\left(v = \frac{Hr \times Hs}{R}\right)$.

(γ) LAWS OF VARIATION OF VELOCITY.—(I) *The greater the cross-sectional area the less the velocity, and conversely.* (II) *The greater the activity of the heart as to rate or strength or both, the greater the velocity.* (III) *The greater the peripheral resistance the less the velocity.*

4. **The Circulation Time.** (*a*) **Method of Determination.**—Early methods (Hering, 1829; Blake, 1841; Vierordt, 1858) consisted in injecting a solution of a salt (*e. g.*, ferrocyanide of sodium) into one jugular vein, and testing the contents of the opposite jugular from second to second to determine the time required to make the circuit.

A very ingenious and accurate method devised by Stewart (*Jour. Physiol.*, Cambridge, 1894, vol. xv. p. 1) is described as follows: "The carotid artery is exposed and placed upon a sheet of insulating material; non-polarizable electrodes are then applied to the artery, and the portion of the artery between these is inserted as a resistance in one arm of a Wheatstone bridge. After the resistances in the bridge have been balanced, and the galvanometer brought to rest, a small quantity of a solution of common salt is injected into the opposite jugular vein. So soon as the salt reaches the carotid artery the resistance of the blood is altered, the balance of the Wheatstone bridge is upset, and the galvanometer swings.

"The period between the moment of injection and the commencement of swing can be noted with a stop-watch with great precision."

(*b*) **The Results** obtained by the application of the above methods may be tabulated: It is understood that the time is from the jugular vein of one side to the jugular vein of the opposite side.

ANIMAL.	SECONDS.	ANIMAL.	SECONDS.
Squirrel	4.39	Dog	16.32
Cat	6.69	Horse . . .	31. 5
Rabbit (Vierordt) . .	7.79	Cock . . .	5.17
Rabbit (Stewart) . .	6.00+	Duck	10.64

The results given above are those for the first blood which makes the entire circuit. It is estimated that it requires about five times as long for the whole volume of blood to pass through the left ventricle as it takes for the first portion to make the circuit.

5. **The Pulse.**—Though this topic should logically come under consideration with *Variations of Blood Pressure*, its importance

clinically and the fact that a number of extra factors are involved in it justify a separate discussion.

The determination of blood pressure with the Ludwig or Fick instrument is *immediate* or *direct*, while the determination of the pressure by an examination of a superficially located artery is *mediate* or *indirect*. In the first case the character of the arterial walls or of the tissues overlying the artery cuts no figure, while in the examination of the pulse these are important factors. Until comparatively recently no other means for the examination of the pulse has been used than palpation with the finger-tips; even now this method is most important, and the *tactus eruditus* reveals to the physician all the important variations of the pulse.

(*a*) **Instruments for Recording the Pulsations** of an artery are called *Sphygmographs*. There are several forms. The one in most common use by clinicians is the Dudgeon sphygmograph. An essential feature of this instrument is a system of compound levers which transmits the movement of the arterial wall from the foot or pad which rests upon the skin over the artery to a tracing point connected with the last lever. This system of levers multiplies the motion of the foot about fifty times. A second feature of the instrument is a recording apparatus consisting of a clockwork which turns a pair of small cylinders between which runs a slip of blackened paper. The tracing point rests upon this paper and records there the magnified movements of the foot or pad.

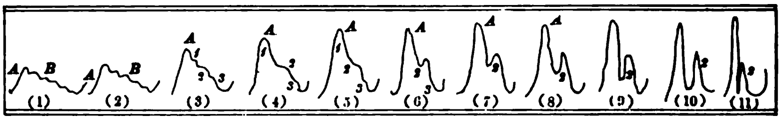
Another form of sphygmograph particularly valuable to the physiologist is the one devised by Professor Porter, of Harvard. The apparatus consists of two tambours, the recording tambour having a very small volume, a very thin membrane, and a long, light lever; while the receiving tambour is larger and modified according to the artery which is to be observed. The record is traced upon a kymograph.

The *Sphygmograph* has the great advantage that it makes a record of the variation of pressure, and when properly used may reveal many facts about the general condition of the circulatory system. The disadvantages of this instrument are that slight variations in the location of the artery in different individuals lead to variations in the tracing; that accumulation of fat on the wrist may also "obscure" the artery, and make the use of the sphygmograph difficult or make the results of no value; and, finally, that faulty adjustments of the instrument lead to widely varying results with the same pulse. When the sphygmograph is used with all its disadvantages known and carefully weighed, or avoided, it may be a most valuable adjunct in physical diagnosis, especially for making a permanent record of a pulse for subsequent reference or comparison.

(*b*) **The Pulse Tracing or Sphygmogram.**—The sphygmogram has been defined by Mackenzie as "a diagrammatic representation of the variations of pressure within an artery." It will be seen at once by reference to Fig. 105 that upstroke *A* and downstroke *B* represent the rise and fall in pressure due to ventricular systole and diastole. Obeying the general laws of liquids under intermittent pressure, the impulse, or *pulse,* is transmitted along the arteries as a wave or undulation of the arterial walls. The sudden upstroke *A* indicates the sudden influx of blood into the aorta during systole, while the gradual fall of the part *B* indicates the gradual fall of arterial pressure during diastole. The small waves, 1, 2 and 3, superimposed upon *B*, are called in order: (1) *Tidal wave,* or predicrotic; (2) *Dicrotic*; (3) *Postdicrotic.* The apex (*A*) is called the *Percussion wave* or *Systolic wave.* The dicrotic wave is due to the closure of the semilunar valves. The predicrotic and postdicrotic waves are due to the elastic tension of the arteries. Once set in motion the wall tends to continue to vibrate under the influence of a series of secondary waves.

It is maintained by some investigators that some of the secondary waves, particularly the predicrotic, are caused by reflection from the periphery. Be this as it may, it is universally accepted that the two *waves of clinical importance*—viz., the *Percussion wave* and the *Dicrotic wave*—are caused by systole and closure of the semilunar valves respectively—*i. e.*, they have their origin at the heart.

FIG. 105



Sphygmograms from normal individuals.

These secondary waves fall into two classes. Fig. 105 gives a series of sphygmograms from normal individuals in widely varying states of blood pressure, the highest pressure being shown in sphygmogram No. (1). From No. (1) to No. (11) the arterial blood pressure is progressively lower, even merging into the pathologic in Nos. (10) and (11), which were taken in the fever stage of acute "cold."

The two classes of superimposed curves come out into prominence in this series: The Predicrotic and Postdicrotic waves as shown in Nos. (3), (4), and (5), which are typical, and average normal tracings, belong clearly to the class shown on the downstroke *B* of Nos. (1) and (2), where no dicrotic wave may be differentiated. There may be four, five, or even six or seven of these wavelets on a high-pressure sphygmogram. They are called "*elasticity waves.*" With gradually decreasing pressure the less tense and very extensible arterial wall shows a decreasing tendency to transmit these waves until finally they are not discernible. The dicrotic wave, however, is more and more pronounced with gradually decreasing pressure. Note wavelet

2 in tracings Nos. (3) to (11). In Nos. (3), (4), and (5), where we have both elasticity waves and the dicrotic on the tracing, the dicrotic is probably a resultant of two causes: (1st) the cause of the second elastic wave and (2d) the closure of the semilunar valves, because there would naturally be an elastic wave at 2 any way, and, beginning with tracing No. (3), some extra cause seems to be operating to emphasize or increase wavelet 2. Finally, in tracing No. (6), the conditions necessary for the transmission of the elasticity waves have disappeared, while the dicrotic continues to increase.

(*c*) **Modification of the Sphygmogram.** (α) LOCAL CONDITIONS.—The percussion wave and the dicrotic wave of the radial sphygmogram are greatly *diminished:* (I) By occlusion of the veins of the arm; (II) by the dependent position of the arm; (III) by plunging the arm into cold water. These primary waves are, conversely, greatly *increased:* (I) by holding the arm above the head; (II) by plunging the arm into hot water.

(β) GENERAL CONDITIONS.—The *dicrotic wave is accentuated* in its relative height *when the arterial pressure is low* because of: (I) *dilated arterioles,* as after a hot bath or in the first stage of asthenic fever; (II) *diminished heart action,* as after severe hemorrhage, or following a forced expiratory effort. The elastic arteries of *youth* show a well-marked dicrotic wave.

(γ) GENERAL SIGNIFICANCE OF THE DICROTIC.—*It is increased at times of exhaustion and diminished at times of vigor* (Schaefer).

(*d*) **Variations of the Pulse Rate** are found to depend upon *age, height, muscular activity, state of the emotions.* Then, besides a certain range of *individual variation* there is a wide range of *pathologic variation.*

(α) Variation with AGE: At birth the rate is 130 to 140. By about the eighteenth year it gradually decreases to the average for adult life, which is from 60 to 75 or not far from 70 per minute. This rate is maintained until the beginning of the senile period, between the fiftieth and sixtieth year, when there is a gradual increase to 80 or more per minute.

(β) Variation with HEIGHT: Short individuals have a faster rate than tall ones; a height of 140 to 150 cm. (4 ft. 8 in. to 5 ft.) corresponding to a rate of 74 per minute while 180 cm. (6 ft.) corresponds to 60 per minute.

(γ) There is a variation of the pulse rate with varying muscular activity, the rate being increased to a greater or less extent by exercise.

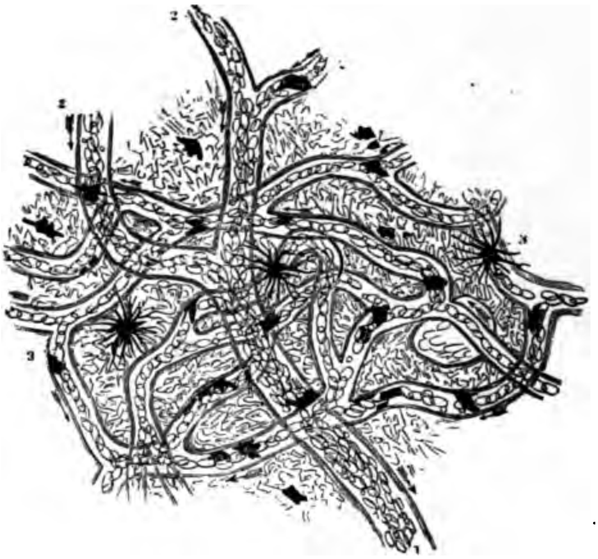
(δ) With emotional excitement the pulse may be greatly increased in rate.

b. The Circulation in the Capillaries.

1. **Cause and Variations.**—The ultimate cause of the blood pressure in the capillaries is, of course, the force of ventricular

systole. Though the capillary pressure, and therefore capillary flow, is ultimately caused by systole, it is immediately varied by change in the lumen of the arterioles. If, for example, the local blood supply is increased by a widening of the arterioles under the influence of the vasomotor nerve-muscle apparatus, then the capillary pressure will be much increased. On the other hand, if the local blood supply be decreased through narrowing of the arterioles, the capillary tension will be much decreased. In the first case the resistance offered by the arterioles is decreased, while in the second case it is increased. But the resistance offered by the arterioles is the variable factor of the peripheral resistance. The greater the arteriole resistance, the less the capillary pressure, and conversely. Or it may be thus stated: The greater the sectional area of the arterioles, the greater the capillary pressure, and conversely.

FIG. 106



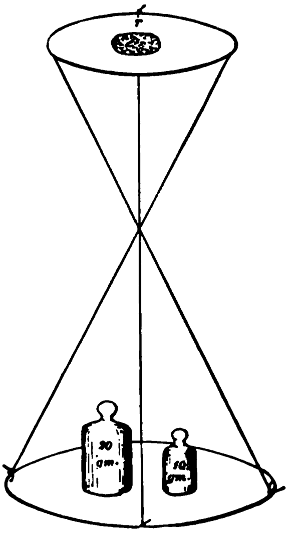
Capillary plexus in the portion of a web of a frog's foot, magnified 110 diameters: 1, trunk of vein; 2, 2, 2, its tributaries; 3, 3, pigment cells; other vessels are capillaries. (Carpenter.)

To sum up, then: *The capillary pressure varies* (I) *directly as the energy of the heart's systole,* and (II) *directly as the sectional area of the arterioles. It may be further stated that the local capillary pressure, and consequently local plasma supply to the tissues, varies directly as the local sectional arteriole area.*

2. **Results.**—This relation between the condition of the arterioles and capillary pressure is a most important physiologic fact. For

a concrete case let us suppose that the blood, rich in foodstuffs from a recent meal, is on its way from the digestive organs to the general system; the individual resumes his work, which, let us suppose, is manual labor involving especially the muscles of the arms; the arterioles of the arms dilate; the local blood supply is much increased, probably doubled; the veins and lymphatics are rapidly emptied by the working of the muscles; with the decreased resistance in the arterioles has come an increase of capillary pressure; the increase is so great that the rich plasma is forced through the permeable capillary walls and bathes the muscle cells. Under such conditions a certain amount of the waste products will enter the capillaries near their junction with the veins, where the pressure is low, but much will also leave the working muscle by way of the lymph radicals and lymphatics; some will be retained, and after a few hours the muscle will be fatigued—a rest is in order. During rest the arterioles contract, capillary pressure falls, and the accumulated products of destructive metabolism readily find their way into the capillaries, are carried to the organs of excretion, and thrown out of the system.

Fig. 107



Apparatus for determining the capillary pressure.

3. **Method of Determining Capillary Pressure.**—Von Kries used a glass plate of known dimensions, to which was hung a scale pan; the weight of the scale pan and plate plus the weight necessary to exclude the blood from the capillaries equals the pressure for the area of the plate. If the area of the plate be 100 square millimetres; if the weight of the apparatus be 5 gms.; if the weight added to suppress capillary circulation be 22.2 gms., and if Pc be the capillary pressure per square millimetre, then $100\ Pc = 27{,}200$ mgms.; $Pc = 272$ mgms. Expressed in height of column of mercury: $Pc = \frac{272}{13.6} = 20$ millimetres of mercury. Several different methods have been used which involve the same principle.

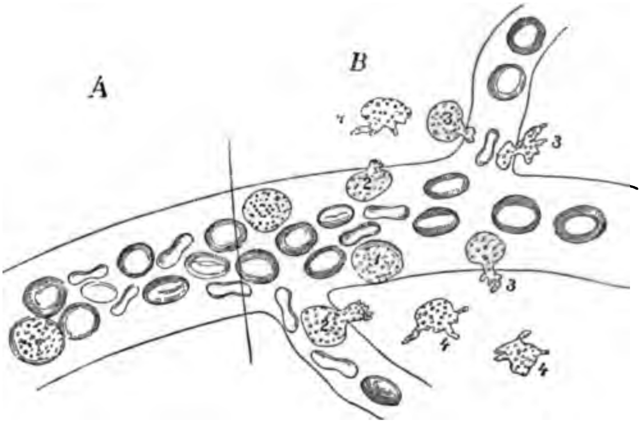
A slight modification of von Kries' method (see Fig. 107) may be used. The plate which rests upon the finger has no raised plate of known area; it therefore becomes necessary to determine the area of the part from which capillary circulation is excluded. Suppose its diameter to be 8 mm.; weight of apparatus, 3.35 gms.; weight added to stop capillary circulation in area exposed, 20 gms.; total weight = 23.35 gms.

From the experiment above cited one may make the following general formula: $Pc = \frac{w}{ag}$ when w = weight in milligrams; when a = area in sq. mm.; when g = sp. gr. of mercury. But a = πr^2, therefore the formula becomes:

$$Pc = \frac{w}{\pi r^2 g} = \frac{1}{\pi g} \times \frac{w}{r^2}$$

But $\frac{1}{\pi g}$ is a constant quantity, w and r only being variable, so that we may give as a general formula for this apparatus: $Pc = K \frac{w}{r^2}$, or *the capillary pressure equals a constant* (0.0234) *multiplied by the weight required to exclude the capillary circulation from an area and divided by the radius of the area squared.* The result thus obtained is in millimetres, and represents the height of a column of mercury which would balance the capillary pressure.

FIG. 108



Diapedesis: 1, adhesion to wall; 2, finding opening by pseudopod; 3, traversing the wall; 4, resumption of active form; A, normal field, showing large capillary with corpuscles in centre of blood stream; B, field of irritation, leukocytes leaving current and sticking to wall, causing a partial blocking of flow of red corpuscles.

The various results of von Kries, Ray, and others vary from 15 mm. Hg to 50 mm. Hg., according to the relation of the various factors involved in the capillary pressure at the time of determination. The position of the part has been found to be an important element. If the hand be held above the level of the shoulder, for example, the capillary pressure will be much decreased.

4. **Diapedesis.** (See Fig. 108.)—The term diapedesis is used to express *the passage of corpuscles through the capillary wall.* The passage of white corpuscles through the capillary wall is a normal

ess, and is the result of an amœboid movement of the leukocyte; the passage of red corpuscles is an abnormal process. The ess may be analyzed into several acts: (i) adhesion to wall; finding of openings by pseudopod; (iii) the amœboid movements flowing of protoplasm incident to traversing the wall; (iv) mption of typical form and migration through tissues. The ense importance of this process was first emphasized by Cohn- ı. In inflammation both red and white corpuscles (but the white far more numerous) migrate in myriads into the tissues. Here white corpuscles may be sacrificed for the good of the organism. l leukocytes are called *pus corpuscles*.

c. The Circulation in the Veins.

Forces Involved in Venous Circulation.—(α) RESIDUUM OF RT PRESSURE exerted through the capillaries.

) NEGATIVE INTRATHORACIC PRESSURE caused by: (i) Action of hragm and other muscles of inspiration. (ii) Ventricular systole, its attendant decrease in the volume of the heart. (iii) Apex , pushing out the anterior wall of the thorax. This negative sure or *suction* tends to lift the column of venous blood in the ominal vena cava.

) MUSCULAR CONTRACTION, through which the increasing girths ne muscles in any functional unit—as the gripping muscles of orearm—cause lateral pressure upon the veins. Through this al pressure the blood is forced out of the veins, whose valves it movement toward the heart only.

) THE FORCE OF GRAVITATION modifies venous flow: (i) *hasten*t in the jugulars and anterior vena cava; (ii) *retarding* it in the rior vena cava, in the veins of the legs, and in the veins of the when these hang down.

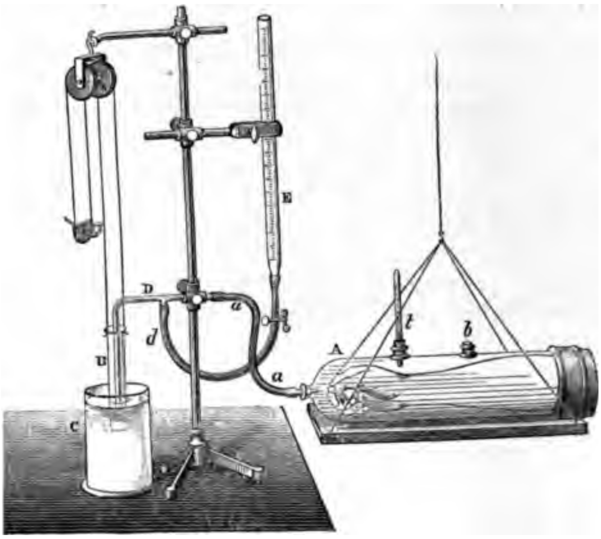
POSITIVE INTRA-ABDOMINAL PRESSURE, during inspiration and ng forced expiration.

these forces the first three (α, β, γ) are the efficient forces of us circulation; the remaining forces are either so small in relation e first three that they may be ignored or they act only as modify- actors or under special conditions. The force of gravitation, gh it assists the downward flow in all veins and retards the rd flow, may rather be recorded among the factors which fy venous circulation. Any action of the walls of the abdominal y (descent of diaphragm in inspiration or contraction of the l walls in expiration) will force toward the thoracic cavity any l in the abdominal veins, but it will, to the same degree, keep f the abdominal veins the blood from the legs.

Variations of Venous Pressure.—The forces involved in venous ation, as enumerated above, are the causes of blood pressure in the veins. These factors vary greatly in different parts of the venous system—*e. g.*, in the venules the principal factor is the residuum of heart force. In the veins of the limbs one important factor is muscle movement, causing a flow toward the heart through a pressure exerted upon the walls of the veins; this increases the pressure within the veins and forces the blood to move in the direction of least resistance.

The distal flow is blocked by the valves of the veins, and the flow toward the heart is thus increased. In the large venous trunks near the thorax the negative intrathoracic pressure—caused by inspiration, by cardiac systole, and by the apex beat—is the principal factor of venous circulation, operating not by causing higher pressure at the periphery, but by causing lower pressure at the centre. The quickening of venous circulation through muscle movements, whether these movements be passive or active, is the basis of the theory of massage. All the varied phases of massage treatment have developed from this point, and all have the effect of quickening venous and lymphatic circulation primarily, and of recuperating and rejuvenating the tissues secondarily. Active muscular exercise not only quickens venous and lymphatic circulation directly in the manner described, but also indirectly through causing an increase in the frequency and strength of ventricular systole, and furnishing a larger residuum of cardiac force for venous circulation.

FIG. 109

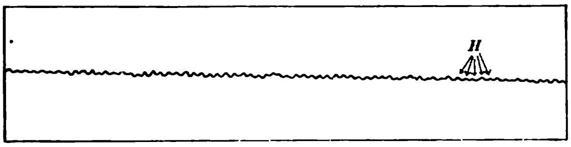


Plethysmograph of Mosso. (Marey.)

3. **The Plethysmograph.**—This instrument comprises a metallic or glass case, which is made to enclose an arm, leg, or finger, the open

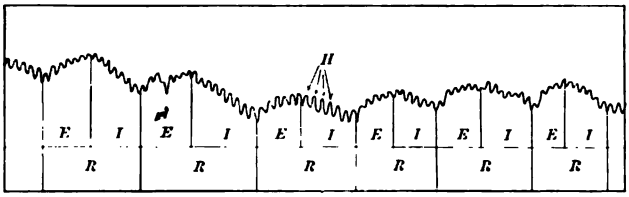
f the case being closed with gutta-percha. (See Fig. 109.) A tube from the plethysmograph connects with a pressure apparatus

FIG. 110



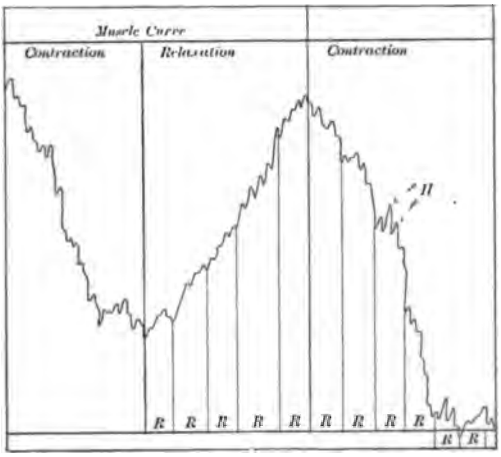
ysmogram. Respiration was suspended. The small waves *H* are due to the influence of the heart alone.

FIG. 111



thysmogram. The influence of respiration is added to that of the heart. *R* indicates respiratory wave; *E*, expiratory portion; *I*, inspiratory portion.

FIG. 112



ysmogram. The influence of muscular contraction is added to that of respiration and ontractions. The arm is emptied and the curve drops during contraction. The respira-ves are well marked in portions of the tracings.

nother with a recording tambour. Any changes in the volume ccurately recorded by the tracing lever upon a kymograph drum.

The accompanying plethysmograms, taken by the author during a class demonstration, show the general influence of the circulation upon the volume of the arm.

These tracings justify the following conclusions:

Fig. 110. The volume of the arm (or other portion of the body) is affected by the cardiac contractions.

Fig. 111. The volume of the arm is influenced by the respiratory movements, being increased during expiration and decreased during inspiration. The reason for the decrease during inspiration is that the increased negative intrathoracic pressure empties the veins of the arm.

Fig. 112. The volume of the arm is influenced by muscular movements, being increased during relaxation and decreased during contraction. The reason for the decrease during muscular contraction is that the pressure of the contracted muscles upon the veins and lymphatics empties them toward the heart. This is a demonstration of the validity of the point given above, where muscular contraction was given as one of the forces which cause venous blood flow.

d. The Coronary Circulation.

The problem of the nourishment of the heart muscle through circulation of blood in the coronary vessels of the heart has led to much controversy.

In 1689 Scaramucci formulated two hypotheses based upon superficial observation and a meagre knowledge of the forces which actuate the circulation. These two hypotheses were: (I) The deeper coronary vessels are squeezed empty by the contraction of the muscle fibres which surround them. (II) The coronary vessels are refilled from the aorta during the diastole of the heart. A few years later Stroem added a further hypothesis: The coronary vessels are filled in diastole because their mouths are closed in systole by the semilunar valves.

Actual experiment in this field is successful only through the aid of delicately adjusted apparatus, accurate observations, and unbiased conclusions.

We need not follow the various phases of the controversy through its two centuries of discussion, largely polemic, but come directly to the presentation of some recent work of the Harvard physiologic laboratory, which seems to settle most of the questions at issue.[1]

1. **Methods of Observation.** (*a*) **Coronary Blood Pressure.**—Dogs and cats were used as subjects of the experiments. The observations were made on anæsthetized animals, whose respirations were carried on artificially through tracheal cannulæ. Blood-pressure observa-

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[1] Porter, Influence of Heart Beat on Flow through Heart Wall, American Journal of Physiology, vol. I. p. 145

tions were made on the left coronary (ramus descendens) and one of the carotid arteries. Simultaneous tracings were made through the use of a Hürthle membrane manometer. This procedure enabled the observers to determine the relation between coronary blood pressure and general arterial blood pressure.

(*b*) **Volume of Coronary Blood Flow.**—"In this experiment the extirpated heart of a cat was fed with warm defibrinated cat's blood from a reservoir at constant pressure through a cannula in the ascending aorta, all the branches of that vessel except the coronary arteries having been previously tied. The blood passed from the coronary artery into the right ventricle, and thence through a glass tube drop by drop upon an aluminium plate fastened upon the lever of a Marey tambour." This device recorded the amount of blood (in drops) passing through the coronary circulation. It recorded also the heart activity.

2. **Results of Observations.**—(I) "Curves of the blood pressure in the carotid and coronary artery, recorded simultaneously by two sensitive membranes, reveal no noteworthy difference in the form (or time) of the pulse wave." (See Fig. 3, p. 152, vol. i., *American Journal of Physiology.*)

(II) "The intramural branches of the coronary vessels are compressed by the contraction of the muscles around them."

(III) "The volume of the blood passing through the coronary vessels is increased by an increase in either the force or the frequency of the heart beat." (See Fig. 4, vol. i., p. 158, *American Journal of Physiology.*)

(IV) "The emptying of the intramural vessels by the contraction of the heart favors the flow of blood through the heart walls chiefly by the diminished resistance which the empty patulous vessels offer to the inflow from the aorta when the heart relaxes.

3. THE CIRCULATION OF THE LYMPH.

a. In the Lymph Radicals.

Causes and Variation.—After the plasma has oozed through the capillary wall and become lymph it receives pressure from three sources: (I) The capillary pressure which caused it to filter through the capillary wall is not all expended in that process; or, expressed differently, as long as more plasma is passing into the tissues, the plasma or lymph already there is forced on through the minute lymph radicals. (II) Endosmosis is the principal physical factor of lymph circulation in the lymph radicals of the intestinal mucous membrane. (III) The physiologic factor *selection* plays a still more important role, but it cannot be measured. Variation of any of these factors—the first through variation of capillary pressure, or the second and third through the conditions in the alimentary canal—will cause a variation of pressure, and, as a consequence, a variation of the flow in the lymph radicals.

b. In the Lymphatics.

Causes and Variation.—(I) *Residuum of the pressure* in the lymph radicals is a strong factor. (II) The most important factor of lymph circulation in the limbs is *muscular activity*. As is the case with the venous circulation, so here the efficiency of muscular activity depends upon the presence of valves within the vessels. The numerous lymphatic glands in the course of the lymphatics—especially in the axilla and groin—act somewhat like valves in staying the reflux of the column of lymph after it has once passed. (III) In all those lymphatics near the *thorax* the *negative pressure* of that cavity during inspiration acts as a strong motive factor. Variation of muscular activity is the most important variable factor in the lymphatic circulation.

E. THE CONTROL OF THE ORGANS OF CIRCULATION.

1. THE INNERVATION OF THE CIRCULATORY SYSTEM.

When we remember that the general flow of blood, in response to arterial pressure, is affected directly by the activity of the heart and reciprocally by the sectional area of the arterioles and capillaries, it is clear that the problem of determining the exact status of the circulation can only be solved by knowing the value of both variable factors, which solution is not facilitated by the fact that both the heart activity and the sectional area of the arterioles are variously affected by different local and general stimuli. These different stimuli affect the circulatory organs usually through the medium of the nervous system, though certain stimuli may act directly upon the muscle tissue of the heart or arteries.

Fig. 113 gives the innervation of the heart. Note that there are two sources for this nerve supply: (I) the vagus nerve, and (II) the sympathetic system of nerves. The cardiac ganglia were once supposed to represent a third and *local* reflex centre, but these ganglia are now known to serve as simple relay stations on the vagus, or inhibitory innervation of the heart.

a. The Innervation of the Heart.

1. **The Action of the Heart Muscle.**—The most recent and authoritative presentation of the action of the heart muscle and the control

that action is that by Gaskell Schafer's *Physiology,* vol. ii. 169 *et seq.* A few quotations ow:

'The ganglion cells in the ırt are part of the great group ganglion cells which are situd on the course of the smallred efferent nerves supplying viscera. These cells form the lying groups of nerve cells ich are known by the name of sympathetic and cerebronal ganglia. In the case of heart the ganglion cells beıg to the small-fibred efferent rdiac fibres of the vagus, just some of the cells in the gangn stellatum and in the inferior rvical ganglion belong to the ıall-fibred efferent cardiac fibres the augmentor nerve. There no more reason to assign spel functions to these cells than any of the other peripheral erent nerve cells. They are ls connected only with the inhiıitory fibres of the vagus, and such are simply part and parof the mechanism of inhibiı, just as the corresponding ls in the ganglion stellatum are ıply part and parcel of the mentor mechanism." (Scha, vol. ii. p. 197.)

'The beat of the heart of d-blooded vertebrates depends on the rhythmic power of the scular tissue of the large veins l sinus being greater than the thmic power of the other parts the heart. In all cases the ater or less rhythmicity of any t of the heart depends upon nature of the muscular fibre which that part is composed,

FIG. 113

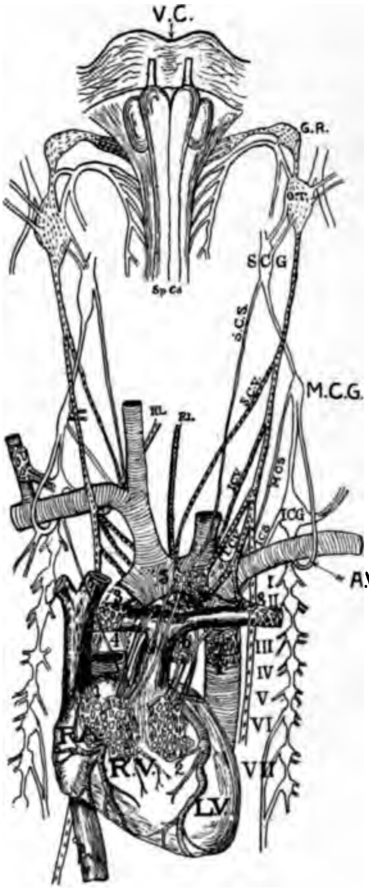

Diagram of the nerve supply of the heart. Dotted lines show vagus origin of cardiac plexus; continuous lines show sympathetic origin of that plexus. *VC*, vagus centre in floor of fourth vent.; *SCS*, cardiac branch of the sup. cerv. symp.; *MCS*, cardiac branch of the mid. cer. symp.; *I* to *VII*. rami communicantes from spinal cord to ggl. of symp. syst.; *ICS*, inf. cerv. symp. cd. br.; (3) coronary plexuses are really div. of the gen. cardiac plexus; *TCV*, thoracic card. br. of vagus; *GR*, ganglion of vagus root; *GT*, ganglion of vagus trunk; *SCV*, sup. cardiac br. vagus; *ICV*, inf. cardiac br. vagus; *RL*, recurrent lary., giving branch to cardiac plexus; *GCP*, great card. pl. of vagus and sympathetic fibres; *SCG*, superior cervical ggl. symp.; *MCG*, med. cervical ggl. symp.; *ICG*, inf. cervical ggl. symp.; *StC*, stellate gang. sympathetic; *A Vs*, annulus of Vieussens around subclavian artery.

and not upon the presence or absence of ganglion cells." (Schafer, vol. ii. p. 180.)

"The sequence of the contractions of the different parts of the heart is most probably due to the passage of a wave of contraction along muscular tissue, though under certain conditions this contraction may be so small as not to be visible by ordinary methods of investigation.

"The causation of the beat of the heart and of the sequence of the contractions of the separate cavities is the same in warm-blooded as in cold-blooded animals." (Schafer, vol. ii. p. 186.)

"1. The strength of the contraction does not vary with the strength of the stimulus. The heart's motto, as Ranvier and Kronecker and Meltzer put it, is 'All or none;' either it will not contract at all, or it will contract to the fullest extent possible at the time, whether the stimulus be weak or strong.

"2. The cardiac muscle cannot be tetanized.

"3. The cardiac muscle possesses a long refractory period.

"These three facts of stimulation of cardiac muscle are due almost certainly to one common cause, and to that same cause is due in all probability the rhythmic power of the cardiac muscle and the peculiarities of the conduction which are manifested in the due sequence of the contraction of the various chambers." (Schafer, vol. ii. p. 189.)

"Efferent fibres of opposite function leave the central nervou system to supply the viscera; they pass out of the central nervou system as the fine medullated processes of nerve cells in the centra nervous system. These nerve fibres, the preganglionic fibres, do no pass directly into the tissue of the peripheral organ, but each on terminates in connection with an efferent nerve cell, from which number of fibres, the postganglionic fibres of the same physiologi value, pass to the tissue. The efferent nerve cells of the augmento system are situated in the ganglia of the so-called sympathetic system the corresponding efferent nerve cells of the inhibitory system ar situated in the heart itself." (Schafer, vol. ii. p. 202.)

"1. The rhythmicity of the cardiac muscle varies inversely as it conductivity.

"2. The rhythmicity of the cardiac muscle varies directly as it excitability.

"3. The rate of recovery of the excitability, after a contraction varies directly as the rate of recovery of the conductivity after contraction.

"In other words, the most quickly contracting parts of the hea are the least rhythmic, and, conversely, a block in the passage of th contraction wave is most likely to occur in the more rhythmic tissue

"The end result of the different modifications of the different part is not only to form an efficient force-pump the different chambers o which shall always act in regular order, but also, as Engelmann[1] has pointed out, to render as harmless as possible to the economy any accidental irregularity in the beat of the pump. For we see from his experiments that not only does a contraction travel at different rates over the different muscular tissues of the heart, but also the rate of travel in any one tissue depends upon the phase of that tissue at the time. For just as the excitability of the tissue is restored gradually after a contraction, so also is the restoration of the full power of conductivity a gradual one after a contraction. It follows, therefore, that an interpolated wave of contraction, starting at the sinus soon after a normal contraction, will travel to the ventricle over tissue which has not yet regained its full power of conduction, and consequently will take a longer time to reach the ventricle than the previous normal contraction wave. Therefore, the time between the normal and interpolated ventricular contractions will be longer than the time between the normal and interpolated contractions of the sinus; in other words, any irregularity in the beat at headquarters will tend to be compensated by the time the ventricle contracts, so that the contractions of the ventricle will occur at much more regular intervals than those of the sinus. Seeing that the main importance to the economy is to ensure a regular ventricular beat, it is clear that this more or less complete obliteration of any irregularity in the rhythm, by means of the varying rates of conduction at different phases of the beat, is a very important factor in maintaining the efficiency of the heart." (Schafer, vol. ii. p. 194, 195.)

2. The Regulation of the Heart by the Central Nervous System.—If the cardiac plexus of a dog be followed upward from the mouth of the anterior vena cava it will be found to represent two symmetrically located sources, one to the right and one to the left. If we follow the left we shall find the three or more nerve trunks converging toward the inferior cervical sympathetic ganglion. Here there are connections anteriorly along the vagosympathetic trunk toward the brain and laterally *via* the Annulus of Vieussens, to the first thoracic ganglion of the sympathetic. Whether these connections represent *afferent* or *efferent* nerves is impossible to determine by other means than by physiologic experimentation. Suppose the vagosympathetic trunk be divided high up in the neck and the distal end stimulated with an induction current, the result will be a slowing or stopping of the heart beat; if the stimulation be made lower down and at different points the result will be the same until the inferior cervical ganglion is reached, when the results will be variable and ambiguous. If the Annulus of Vieussens be divided and the distal ends stimulated, there will be either acceleration of the *rate* of beat or augmentation of the *strength* of beat of the heart. If the Rami Communicans II or

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[1] Arch. f. d. ges. Physiol., Bonn, 1897, Bd. xiv., S. 153.

III be divided and stimulated distally, there will be acceleration or augmentation of heart activity. From these experiments we may conclude that the vagosympathetic trunk (in man the vagus) contains fibres whose stimulation causes slowing or INHIBITION of the heart beat, while the sympathetic contains fibres whose stimulation has the reverse effect—*i. e.*, that of ACCELERATION or AUGMENTATION. Through further experimentation the *inhibitory* fibres may be traced along the vagus through the jugular foramen, along the trunk of the spinal accessory to its origin in the floor of the fourth ventricle in the posterior part of the medulla oblongata. In a similar way the accelerator fibres may be traced through the Rami Communicantes, along the anterior nerve roots into the spinal cord, and up to the medulla oblongata, where its exact origin has not been determined. In man the main cardiac branch of the sympathetic is called N. Accelerans cordis, and is not ensheathed with the vagus in any part of its course.

We have now found that the inherent property of the heart muscle to produce an uninterrupted series of alternating contractions and relaxations is governed by the central nervous system in a way analogous to the way in which a horse is governed by the driver; the inhibitory vagus fibres checking the speed of the heart beat and the acceleratory fibres of the sympathetic stimulating the heart to greater speed, or greater force, as the case requires. But what causes the central nervous system to send these messages of inhibition or augmentation to the heart? Here we must recall the general principle that *all messages sent out from the central nervous system*—all efferent nerve impulses—*are in response* (I) *to afferent nerve impulses,* brought to the central nervous system through nerves which carry impulses only from the periphera to the centre—the sensory nerves; (II) to direct stimulation of the centre. As an example of (I) the sudden withdrawal of the hand from a needle point is accomplished through contraction of muscles in the arm in response to an efferent motor message from the centre, which in turn is stimulated by the afferent message of pain from the skin, reaching the centre through a sensory nerve. If we look for the afferent nerves—sensory nerves—which carry messages to the centre from the heart or some part of the periphery, we shall find them represented by only the general sensory nerves, either spinal or sympathetic, and these affect the heart beat only indirectly, after a too complex intercentral interchange to be accepted as a simple reflex. We must look for another way in which the centre may be affected. (II) The *centre* may, however, be *directly stimulated.* Physiologic examples of the direct stimulation of a centre are not numerous and are confined for the most part to the circulatory and respiratory centres. This direct stimulation of respiratory and circulatory centres is made possible by the fact that the activity of these organs is directed toward the supply of the system with blood sufficient in quantity and proper in quality. The nerve centres in the medulla being a part of the system so supplied, are at once affected by variations in blood pressure or in the quantity of CO_2 and of O brought by the blood supply.

(*a*) **Stimulation of the Cardioinhibitory Centre Followed by Slowing of the Heart Beat.** (*α*) DIRECT.—(I) Sudden anæmia of the medulla oblongata, as would be produced experimentally by ligation of the carotids and vertebral arteries. (II) Sudden venous hyperæmia in the medulla oblongata, as would be produced experimentally by ligation of the jugular veins. (III) By increase of the CO_2, as would occur in suspended respiration; thus, any interference with a proper oxygenation of placental blood during pregnancy or parturition will cause a slowing of the fetal heart beats. (IV) Increased blood pressure in the cerebral arteries.

(*β*) INDIRECT.—Strong stimulation of any sensory nerve—*e. g.*, tapping the exposed intestines of a frog with a scalpel handle will cause inhibition of the heart.

(*b*) **Stimulation of Cardioaccelerator**, or cardioaugmentor centres, followed either by aceleration of rate or augmentation of force, or both.

Stimulation may be direct or indirect, but uncertainty about the location of the centre confines our knowledge to that gained by a stimulation of accelerator fibres which always, of course, causes acceleration or augmentation of heart activity with associated rise in blood pressure. Indirect stimulation of the cardioaccelerator centre is illustrated in the sipping of cold water, which has a strong accelerating effect upon the heart, probably through stimulation of the cardioaccelerator centre, through afferent fibres of the sympathetic nervous system.

3. **The Mechanical Stimulation of the Heart.**—(*α*) Through increased flow of blood to the heart due to negative introthoracic pressure. This increase of blood in the heart cavities seems to stimulate it directly without the intervention of the nerve apparatus.

(*β*) Through increased resistance in the aorta; due in turn to increased peripheral resistance.

b. The Innervation of the Arteries.

Though the arterioles and small arteries may change their calibre through such local influences as changes in temperature, their variations in calibre are, for the most part, due to the influence of nerves upon the circular muscle fibres. The nerves which control the arterial supply of the muscles are called VASOMOTOR NERVES. Experiment has proven that there are two kinds of nerves supplying the arteries, as there are two kinds of nerves supplying the heart: (I) There are fibres which augment the tonicity of the vessels by causing contraction; these nerves are called VASOCONSTRICTOR NERVES. (II) There are fibres which inhibit the stimulus given to the muscles by the vasoconstrictor nerves, these are called VASODILATOR NERVES. To get a clear idea of the action of vasoconstrictor and vasodilator nerves it is necessary to take a concrete case. The *submaxillary salivary gland* is supplied by two nerves: (I) a branch of the sympathetic which accompanies the artery; (II) the chorda tympani nerve. Both of these nerves supply fibres to the arterioles of the gland. Under the influence of the sympathetic the arterioles are kept usually in a state of moderate contraction called "tonus." This condition of tonus, which is the usual condition of all the small arteries and arterioles of the body, is maintained by rapidly repeated moderate stimuli passing from the vasoconstrictor centre in the medulla oblongata out to the arteries in all parts of the body. If these stimuli are increased or decreased the tonus becomes higher or lower accordingly—*i. e.*, the vessels are constricted by the contracting circular muscles, or they are dilated by the blood pressure after relaxation of the circular muscles. To return to our example—the arterioles of the submaxillary salivary gland are governed by the general condition of the vasoconstrictor apparatus; and, according as the general tonus is high or low, the local blood supply will be under higher or lower pressure, but not necessarily modified in quantity. If an especially free local blood supply be necessary—as is the case when the gland is actively secreting—some local inhibitory influence must be brought to bear upon the vasoconstrictor nerves to suspend their action and to allow the arterioles to dilate widely under the influence of the blood pressure. This local inhibitory influence is furnished by the chorda tympani nerve, which is called a vasodilator and has upon the muscular tissue of the arteries an influence analogous to that which the vagus has upon the muscle tissue of the heart. From this it would seem that the primary function of the vasoconstrictor nerves is to govern general blood pressure through general changes in the tonus of the small arteries and arteriole, thus increasing or decreasing terminal resistance.

The above example further indicates that the primary function of the vasodilator nerves is to control local blood supply through suspending the action of vasoconstrictors, thus allowing the bloodvessels to dilate. This is in general the relation of the two systems of vasomotor nerves.

1. **The Vasoconstrictor Muscle-nerve Apparatus: Tonus of Bloodvessels.**—The vasoconstrictor centre was located by Ludwig and his pupils in the floor of the fourth ventricle—in the medulla oblongata. That this is a general centre is proven by this experiment. Stimulation causes general contraction of all the arteries; while paralysis of the centre, as by overstimulation, causes general dilatation. From this centre nerve fibres pass down the lateral tracts of

the spinal cord, from which they emerge through the anterior nerve roots and pass into the sympathetic system through the rami communicantes. From the sympathetic system they supply all arteries of the body cavity and some of the arteries of neck and mouth as branches of that system; while the arteries of the skeletal muscles and skin are supplied by branches which have left the sympathetic system and are distributed along with branches of the spinal or cranial nerves. Besides this general centre in the medulla there are local centres in the gray matter of the spinal cord; further, some of the ganglia of the sympathetic system may act as local centres. The action of the local centres may cause a local change in arterial tonus.

(*a*) **Direct Stimulation of the Vasoconstrictor Centre.**—(I) An excess of CO_2 in the blood supplying the centre acts as a stimulus and causes a constriction of the arteries in general. (II) Sudden anæmia of the medulla as the effect of a severe hemorrhage or of ligation of the arteries bringing the local supply. (III) Venous hyperæmia as the effect of the ligation of the jugulars. It is probably the excess of CO_2 which is active in this case. (IV) Poisons—*e. g.*, strychnine, nicotine, etc.

(*b*) **Reflex Stimulation.**—(I) Through "*pressor*" afferent nerve fibres whose stimulation may cause a reflex constriction of the arteries generally. (II) Through "*depressor*" afferent nerve fibres. These are not widely disseminated; most of them are located in the depressor nerve (superior cardiac in man), which passes upward from the ventricular walls, through the vagus to the vasomotor centre. The ventricular termini of this nerve are stimulated by an excessively high arterial pressure. The return message is not sent to the heart, but to the vasoconstrictors of the abdominal cavity, and takes the form of an inhibition, in consequence of which the arteries of the abdomen relax, the blood pressure falls, and the heart is relieved of its excessive work.

2. **The Vasodilatation.**—That there is a system of nerves passing out from a special centre, whose function is to suspend or inhibit locally the general action of the vasoconstrictor system is abundantly proven by such physiologic experiments as that upon the submaxillary gland. It has been further proven that the centre is in the medulla—or at least above the spinal cord—but its exact location has not been determined. The distribution of the vasodilator fibres is in a general way parallel to that of the vasoconstrictor fibres; they may supply a particular locality in the same trunk with vasoconstrictor, motor, and sensory fibres, or they may form a separate nerve, as in the case in the chorda tympani. All vasomotor fibres are efferent; the afferent member of the reflex arc is represented in part by the blood supply of the centre in the case of the vasoconstrictor centre. This condition is possible in that case because the influence of the vasoconstrictor system is for the most part general; but the

local action of the vasodilator system makes direct stimulation of the vasodilator centre practically impossible. As no afferent vasodilator fibres have been found, it is probable that the afferent member of the arc is represented by the sensory nerve coming from any given locality.

2. ADAPTATIVE CO-ORDINATION OF THE ACTIVITIES OF THE CIRCULATORY ORGANS.

In our study of *motion* in general physiology we found that a successful adaptative motion must be co-ordinated in time, or in space and time, and controlled in force. In the same way the activities of the circulatory organs, depending, as they do, upon muscle contractions, must be *perfectly co-ordinated in time* and controlled in force. This is accomplished, as we have seen, through the central nervous system; its co-ordinating messages are sent to the heart and arteries through augmentor and inhibitory cardiac and vasomotor fibres. Through the agency of this most complicated nerve apparatus the following general adaptative adjustments are accomplished:

I. Regulation of temperature.
II. Regulation of secretion and excretion.
III. Regulation of supply of food and oxygen to working organs.
IV. Regulation of general blood pressure.
V. Regulation of local blood flow: To secreting glands; to working organs; in blushing; in pallor, etc. Most of these will be discussed under different headings.

PATHOLOGIC PHYSIOLOGY OF THE BLOOD.

INTRODUCTION.

The blood is quite a stable fluid and changes little except in diseased conditions. The amount of hæmoglobin and the number of leukocytes are most easily affected. The fluid portion of the blood is kept nearly constant in quantity by the easy transmission of lymph, according to osmotic and arterial pressure governed by the nervous mechanism of the body. The reproductive power of the corpuscle-forming organ is enormous, millions of red blood corpuscles and thousands of white blood corpuscles being reproduced every day. Unless the disease is in the blood-forming organs, nature will supply the demand made by most diseases and keep the blood near normal. The changes that occur in disease are varied and complex in many cases, though in some they are very definite. The following will illustrate the changes that take place in the blood in health and in disease.

A. CORPUSCLES.

1. THE RED CORPUSCLES.

a. Morphology.

1. **Form.**—The normal red corpuscle is called an erythrocyte or normocyte (Plate I., Fig. VIII, *a*). One that is smaller is called a microcyte (*h*) and one larger a megalocyte (*i*). When the corpuscle is irregular in shape it is called a poikilocyte. This is usually pear-shaped, though it may be oval or any other shape. When a corpuscle of the usual size has a nucleus it is called a normoblast (*j*, *k*). A microcyte having a nucleus is called a microblast (*l*) and a megalocyte a megaloblast (*m*, *n*). Some irregular distortion of the corpuscles usually occurs while spreading blood films. The glass-slide method of spreading may make the corpuscles oval, but they would all lie in the same direction, which does not occur when produced by disease.

Poikilocytosis (*d*, *g*) is a beginning degeneration of the red corpuscles, and is characteristic of the more severe forms of anæmia, as pernicious anæmia and leukæmia. The oval-shaped poikilocyte is said to be characteristic of pernicious anæmia.

2. **Size.**—The microcyte is any corpuscle smaller than a normal-sized corpuscle, and usually varies from 3μ to 6μ. The megalocyte is one that is larger and varies from 9μ to 20μ. In the milder forms of the severe anæmias the poikilocytes are of the smaller variety, while in the more advanced conditions they are of the larger variety. The presence of a nucleated corpuscle in the blood shows the effort on the part of nature to supply a deficiency, as the corpuscle normally loses its nucleus before it enters the blood stream. Normoblasts are found in the blood in mild anæmias of hemorrhagic or other origin, especially early in life. In the severe forms of anæmia the megaloblasts are more common and significant than the microblasts. The megaloblasts in a beginning severe anæmia contain an increased amount of hæmoglobin, while in the more chronic and advanced stages the amount is diminished. This shows that nature tries to supply a greater oxygen-carrying area by supplying larger corpuscles.

b. Color.

All the color tests show the percentage of color in the whole blood. But as the coloring matter is contained entirely within the red corpuscle, and as these comprise only 50 per cent. of the whole blood, the usual tests are correct only when the amount of corpuscles is normal. The true percentage or color index then will be the amount of coloring matter in each corpuscle.

1. **Hæmoglobin Increased.**—The hæmoglobin is increased in the unusual condition of living in a high altitude, but as the number of red corpuscles is increased in greater proportion than the coloring matter, the color index is low. In pernicious anæmia the amount of hæmoglobin in each corpuscle is increased, although the number of corpuscles is greatly diminished, thus making the color index high, although the percentage of coloring matter in the whole blood is low. The only way more hæmoglobin than normal can be present in the corpuscle is by the corpuscle being larger than normal.

2. **Hæmoglobin Decreased.**—The actual and relative decrease of hæmoglobin is the most common abnormality of the blood. This occurs as a symptom of a multitude of conditions ranging all the way from a lack of fresh air and exercise, intestinal disorders, either of assimilation or elimination, to the severe anæmias, as chlorosis, pernicious anæmia, etc., and is due directly to the excessive loss of iron or the inability to absorb it from the intestinal tract.

c. Number.

1. **Increased.**—An increase in the number of red corpuscles may temporarily be caused by anything that causes a great loss of the plasma of the blood, as severe sweating, diarrhœa, etc. Under the unusual condition of life in a high altitude the corpuscles are increased two or three millions in number, according to the altitude. This is due probably to the lessened atmospheric pressure and to the increased arterial tension, but just how this acts is unknown. The increase, however, is relative only, the volume of the corpuscles remaining the same as before, as the individual corpuscles are smaller. In some forms of anæmia, especially that occurring in young women, called chlorosis, nature attempts to counteract the loss of the oxygen-carrying power of the blood by increasing the number of corpuscles one or even two millions.

2. **Decreased.**—The red corpuscles are decreased in number in all kinds of hemorrhages, epistaxis, menorrhagia, hæmoptysis, hæmatemesis, traumatic hemorrhages, etc. In all forms of blood diseases except chlorosis the number is decreased, as in pernicious anæmia, leukæmia, malaria, etc. In all fevers and acute diseases there is great destruction of red corpuscles causing a diminished number. For example, the exanthemata, typhoid fever, and inflammatory diseases. Also in all wasting and chronic diseases, as diabetes, chronic nephritis, cancer cachexia, etc., the number of red corpuscles is gradually but greatly diminished.

2. THE WHITE CORPUSCLES: LEUKOCYTES.

Number.

1. **Increased.** (*a*) **Simple Leukocytosis.**—Consists of a relative increase of all the different kinds of white corpuscles, and occurs in such physiologic conditions as those following digestion, exercise, short cold baths, or during pregnancy, parturition, early life, and just preceding death. The number under these conditions is usually less than 20,000.

(*b*) **Mononuclear Leukocytosis** *occurs physiologically in infants and young children.* Pathologically it occurs in *cachectic conditions* and in individuals poorly nourished. It occurs in the severe anæmias, as *chlorosis* and *pernicious anæmia,* also in *secondary anæmias* of syphilitic or tuberculous origin. It is present also in *pertussis, hereditary syphilis,* and in *chronic diseases* of the spleen or lymphatic glands. A mononuclear leukocytosis associated with enlargement of the lymphatic glands is characteristic of *lymphatic leukæmia.*

(*c*) **Polynuclear Leukocytosis, or Neutrophilia.**—Practically all inflammatory leukocytoses are of this variety, and vary according to the intensity of the inflammatory process, or the resistance of the patient. Because of this variation the resistance of the individual can be shown by the leukocytosis. In a mild infection a small leukocytosis shows good resistance, while a larger leukocytosis out of proportion to the infection shows poor resistance. In a severe infection a pronounced leukocytosis shows a good resistance, while a poor resistance is shown by no leukocytosis. Among the most important causes of a severe leukocytosis are any *septicæmic* or *pyæmic infection, acute articular rheumatism, pneumonia,* etc.

There is another class of lukocytosis called *toxic,* caused by poisoning with CO, ptomains, tuberculin, prolonged chloroform narcosis, etc. There are some peculiar exceptions to these causes of leukocytosis, as its absence in typhoid fever, influenza, measles, tuberculosis, and some other diseases, until inflammatory complications give rise to it.

(*d*) **Eosinophilia** *consists of an increase in the number of eosinophiles.* This occurs physiologically in infants and during the menstruation of women. Pathologically it occurs in many acute and chronic skin diseases, as eczema, urticaria, and psoriasis; in helminthiasis, as trichinosis and ankylostomiasis; in postfebrile conditions, in malignant diseases, in disease or extirpation of the spleen, in purpura, hemorrhagic exudations, phosphorus poisoning, bronchial asthma, and in myelogenous leukæmia.

(*e*) **Myelæmia.**—The myelocyte (Plate I., Fig. I, *d,* Fig. VII) is an inhabitant of the bone-marrow. The presence of myelocytes in the blood in large numbers occurs in myelogenous leukæmia. In most cases of marked leukocytosis, or severe anæmia, there are a few myelocytes. Myelæmia seems to be the result of stimulation of the bone-marrow.

2. **Decreased.**—A decreased number of leukocytes, or leukopenia, may be caused physiologically by prolonged cold or hot baths, or starvation and malnutrition. Pathologically those diseases mentioned having an absence of leukocytosis where we would expect it frequently have a diminished number, associated with a mononuclear leukocytosis. In severe secondary anæmias, in pernicious and splenic anæmias, the leukocytes are decreased.

The eosinophiles are decreased during digestion and severe exercise. In most cases of leukocytosis they are diminished.

The definite causes of the increase or decrease of the various kinds of leukocytes are known only in a general way. A single or a mononuclear leukocytosis is caused by changed physiologic conditions, such as pressure and osmosis, or by changes in metabolic processes. But to the polynuclear leukocytes it seems that the phagocytic, bactericidal, and chemotactic powers belong pre-eminently. Eosinophilia appears to be caused by a selective chemotaxis.

B. PLASMA.

1. WATER.

The fluid portion of the blood is increased by anæmia and by such conditions as dropsy and anuria. Physiologically it may be caused temporarily by taking large quantities of liquids or by transfusion of saline solution. The fluid portion is decreased by excessive perspiration, vomiting, diuresis, profuse diarrhœa, or extensive effusions.

2. SALTS.

1. *The chlorides* are decreased during febrile diseases, but when the crisis takes place the chlorides are increased, especially in pneumonia. A part of the chlorides are retained in the exudate and another part by the excess of nitrogen from torn-down tissue during the febrile attack. Chlorides are also diminished in the blood in dropsy by being retained in the collections of fluid.

In diabetes insipidus and when diuresis has been established in dropsy the chlorides are in excess.

2. *The phosphates* are diminished in gout, Bright's disease, and in most acute diseases. They are increased in diffuse disease of nerve centres or diffuse disease of bone as in osteomalacia and rickets; also in phosphatic diabetes as described by Tessier.

3. *The sulphates* are physiologically increased by active exercise and a meat diet. In disease they are increased especially in menin-

gitis and rheumatism. In other diseases they increase much as urea does.

4. *Calcium salts* are sometimes increased in gout, when there are calcium concretions; they are diminished in hæmophilia. Theoretically we would expect them to be diminished in osteomalacia and rickets.

3. EXTRACTIVES.

1. *Dextrose* is in excess in the blood in diabetes because of its excessive manufacture due to diseased conditions.

2. *Urea* is physiologically increased by excessive mental or muscular exercise and an exclusive meat diet. It is increased in all febrile conditions because of the increased katabolism. It is also increased in structural disease of the kidneys because its elimination is impeded. It is diminished in malnutrition when metabolism is retarded and also in structural disease of the liver, because its manufacture is diminished.

3. *The purin bodies* are increased by a meat diet associated with limited exercise. They are increased in heart and lung diseases or any condition that lessens the oxygen-carrying power of the blood. They are also increased in acute febrile conditions, lukæmia, and Bright's disease. In general, the purin bodies are diminished whenever urea is diminished.

C. COAGULATION FACTORS.

1. *Fibrinogen* is increased in most inflammatory and infectious diseases. In general it increases as the leukocytosis increases. Fibrin does not increase in malignant disease, tuberculosis, typhoid fever, the severe anæmias, purpura, etc.

2. *Thrombin* is diminished in the hemorrhagic diseases, especially hæmophilia, as the blood platelets are diminished in most of these conditions.

3. *The calcium salts* were mentioned under salts.

THE PATHOLOGIC PHYSIOLOGY OF THE CIRCULATORY ORGANS.

INTRODUCTION.

In the chapter on physiology of circulation it has been shown that the principal functions of circulation are (1) to carry a supply of oxygen and nutritious substances to all the tissues in the body, and (II) to carry CO_2 and other waste products to the organs by which they are eliminated. Further, it has been shown that there are several factors which make possible the transmission and interchange of life-giving and waste products: These are (I) the circulating media, lymph and blood; (II) the propelling organ, the heart, and (III) the circulating channels through which the media pass. A consideration of the pathologic physiology of the circulating media is presented in another section, hence the following pages will be devoted to a consideration of those pathologic processes which clearly interfere with the functions of the heart and the vascular channels. In considering these pathologic states, it will be observed that many important lesions are unaccompanied by subjective symptoms; this is due to the power of the heart to carry on a circulation adequate to the wants of the organism even though the arterial resistance is increased and the valvular and muscular tissues of the heart are diseased. In other words, morbid conditions are productive of physiologic changes which make it possible for the heart to functionate properly. In this chapter the principal morbid conditions arising in the vascular system will be discussed, and their symptoms and progressive pathology explained.

1. PERICARDITIS.

a. Acute.

1. **Pathology.**—The various forms of pericarditis may be considered as different stages of the same pathologic process. In the early stage there is hyperæmia and a rough and lustreless appearance of the pericardium, then an exudate of fibrin finds its way through the diseased pericardial membrane, and this may be followed by an effusion of serum, which may either be absorbed, leaving bands of adhesions, or become infected with pyogenic micro-organisms.

2. **Symptomatology.**—The symptoms of pericarditis are not clear-cut and definite, and in many cases its presence is recognized, if at all, only by physical findings. However, some symptoms are fairly constant in cases that are at all marked. Among these are: chill, fever, pain and discomfort in the pericardial region, distention of veins of neck, aphonia, dysphagia, cough, dyspnœa, cyanosis, restlessness, insomnia and even delirium and coma.

3. **Physiology.**—The *chill* and *fever* point to the *infectious origin* of the disease. *Pain* and *discomfort* are due to irritation of nerve trunks or endings by the inflammatory reaction or distention of the pericardial sac with effusion. The presence of a large effusion prevents a free relaxation or diastole of the heart. This decreases the amount of blood which passes through this organ to the pulmonary

and systemic circulations, and causes the dyspnœa and cyanosis. This disturbed circulatory condition may also be responsible for the restlessness and insomnia which probably indicates an improper blood supply to the brain. The distention of the pericardium may cause (I) aphonia by pressure on the recurrent laryngeal; (II) cough, through irritation of tracheal nerves by compression; (III) dysphagia, through pressure on œsophagus; (IV) enlarged veins on the neck—these from failure of the heart to pump the blood through the pulmonary circulation as rapidly as it returns from the system. Delirium and coma are probably results of toxæmia acting on the brain.

b. Chronic Pericarditis or Sequelæ of Acute Pericarditis.

The pathology is comprised in adhesions between visceral and parietal pericardial membranes, or this plus adhesions to pleura and extension to peritoneum involving liver and spleen. This results in hypertrophy and dilatation.

The symptomatology and physiology of these conditions will be considered under a separate head.

2. MYOCARDITIS.

a. Acute.

1. **Pathology.**—The pathology of myocarditis is typical of inflammatory diseases anywhere, and comprises infiltration of the heart substance with red and white blood cells, fibrin and serum, swelling, granular and fatty degeneration of muscle fibres, and probable pus formation, resulting in small myocardial abscesses. These may rupture into the heart, causing septic emboli, into the pericardium, causing septic pericarditis, or they may be absorbed and leave cicatricial scars.

2. **Symptomatology.**—The symptoms are very indefinite and uncertain; in fact, the disease is not suspected in the great majority of cases, since the symptomatology of the accompanying and causative disease overshadows the heart symptoms. There may be pericardial pain, weak, irregular heart action, and symptoms of septicæmia—these are only suggestive, not positive, and a diagnosis is very unusual.

3. **Physiology.**—The pain is very probably due to the involvement of the pericardium. The degenerating process involving the musculature of the heart would account for the irregular and weakened heart action, since a degenerating muscle fibre would be unable to respond normally to stimulation. Septicæmic symptoms would come from the rupture of myocardial abscesses into the heart cavities; these throw micro-organisms into the blood current.

b. Chronic.

1. **Pathology.**—This disease is characterized by a variety of pathologic findings, all of which are the direct or remote result of impaired circulation in the heart wall. The muscle fibres may show fatty or granular degeneration, and, finally, formation of scar tissue; rupture or aneurysm of the heart may result. Generally these changes are due to obstruction of a coronary artery or some of its branches.

2. **Symptomatology.**—If any symptoms are to be observed they are slow, irregular heart action, and dyspnœa. Other symptoms, those of insufficiency, arise as the compensation is broken, and will be presented under dilatation.

3. **Physiology.**—It will be readily observed that a muscular tissue whose substance is honey-combed and even partly replaced with an unusual amount of fibrous tissue will contract much less easily and rapidly than as of one in normal condition. Part of its energy must be expended in overcoming the resistance of the fibrous tissue. This causes the slow, irregular heart. The dyspnœa probably results from failure of the heart to pump the blood through the lungs fast enough to ensure proper aeration.

3. ENDOCARDITIS (ACUTE).

1. **Pathology.**—The pathology is not uniform, but the inflammatory changes most frequently affect the endocardium lining the valves. There is first a swelling of the basement membrane and œdema of the endothelium. There may be irregular proliferations of the former, in which case outgrowths or vegetations appear. If from any cause degeneration should occur, ulceration ensues. In any case, if roughing of the surface occurs, fibrin, blood platelets, and other elements of the circulatory medium are prone to become attached to this rough spot and help form the vegetations which in this are really fibrous-tissue outgrowths.

In the so-called malignant endocarditis all the above lesions may be observed, more marked, perhaps, than there presented, but the great difference lies not in the form of the lesion, but in the presence of bacteria in and on the vegetations. Further, there may be septic embolic processes in different parts of the body.

2. **Symptomatology and Physiology.**—In view of the fact that acute endocarditis is a disease complicating a great number of systemic infections and diseases of uncertain origin, its symptomatology is too vague and diverse to admit of positive classification and explanation. There is usually a febrile reaction and increase in pulse rate, but to what extent this may result from the endocarditis or from the accompanying (or causative) disease cannot be definitely

stated. About the only definite symptoms in the course of an attack of malignant or ulcerative endocarditis are those arising from emboli which are detached from the morbid growths on the valves and carried along the blood current, to be lodged in some organ or tissue at a point where repeated subdivision of the artery makes it too small to admit of the passage of the embolus. It will be readily observed that the symptoms in such a case would depend upon the organ or tissue in which the embolus lodged, the size and character of the embolus, and whether a collateral circulation might be easily established.

In this connection it will be well to consider thrombosis and embolism, though these diseases or accidents do not of necessity accompany acute endocarditis alone, but may be associated with any conditions which cause slowing of the blood stream or roughening of the endothelium.

a. Thrombosis.

1. **Pathology.**—A roughened endothelium, whether of the heart, arteries, or veins, predisposes to a deposit of blood platelets, white cells and fibrin, which form a clot or thrombus on the roughened surface. This may become absorbed or become organized; in the latter case forming a partial or complete plug of fibrous tissue in the lumen of the vessels.

2. **Symptomatology.**—The symptoms vary with the size and location of the vessel affected and are due entirely to mechanical effects unless bacteria should be present. If a coronary artery were affected, there would ensue symptoms of cardiac insufficiency because of failing nutrition of the heart muscle. If a cerebral artery were affected, the symptoms of anæmia and ischæmia of the area supplied by it would gradually supervene. If, however, instead of these end arteries a freely anastomosing vessel should be occluded no symptoms would be noticed. In any of the above cases infected thrombi would be very apt to result in abscess formation, and the symptoms of infected thrombi are so diverse, depending on the part of the body in which they form, that the student must apply his knowledge of inflammation to individual cases, reasoning from cause to effect for each location.

3. **Physiology.**—Relative ischæmia of any tissue or organ lessens its power for work. Absolute ischæmia renders it functionless and entails atrophy and degeneration. These very general statements must be applied to concrete cases.

b. Embolus.

1. **Pathology.**—Emboli may result from a loosened or degenerating thrombus, rupture of a small cyst or abscess into heart, an artery or vein, detachment of a vegetation or the introduction of any foreign

body into the blood stream. The foreign body, for such it is in any case, lodges at the opening of an artery too small to admit of its passage and stops the circulation.

2. **Symptomatology.**—Wherever the embolus may lodge, the primary symptoms are sudden and result from complete ischæmia of the part supplied by the artery. If collateral circulation can be readily established, the symptoms soon abate. If the artery is an end artery with no large anastomosing branches, the tissue it formerly supplied will soon die, atrophy, and degenerate. If the tissue supplied should be heart muscle or brain tissue, death might be almost instantaneous. Infected emboli mean abscesses.

3. **Physiology.**—The physiology of thrombosis is applicable in this disease.

4. ENDOCARDITIS (CHRONIC): VALVULAR DISEASES.

1. **Pathology.**—Following an attack of acute endocarditis or independent of any known acute process, chronic proliferation and degeneration of endocardium are quite common and various morbid conditions may result. There may be nodular thickening of one or more valve segments with a loss of the normal translucency of the membrane. The formation of fibrous tissue, evidenced by the nodules, continues, and finally so distorts the valve that a pure insufficiency or insufficiency with stenosis results. This, with the attendant dilatation and hypertrophy may safely be outlined as the pathologic picture which accompanies acquired valvular disease.

2. **Symptomatology.**—The symptoms are seldom at all marked until loss of compensation occurs; then the symptoms vary with the character of the lesions and valve involved. This brings up for consideration chronic valvular diseases, and these will be presented in as brief a form as possible with a clear understanding of the fact tha any valvular lesion may exist for years and produce no noticeable symptoms—this is due to the ability of the heart muscle to adapt itsel to changing conditions by hypertrophy. Aside from the condition o the affected valve, there are changes in the heart wall and othe valves upon which depend the symptoms. Tracing back against the blood stream from the affected valve, gradual changes will be observed to occur. If the lesion should be aortic insufficiency, great dilatation and hypertrophy of the left ventricle would follow, then mitra incompetence would be very likely to result from the dilatation and hypertrophy of the auricle would ensue. This would cause insufficiency, a damming back or an impediment to the pulmonary circulation, and progressive involvement of right ventricle and auricle and in the extreme case venous stasis. This outline of the possible pathologic changes in the heart walls and valves shows the difficulty

which would beset a student if confronted with a case representing combined lesions, hence, though not true to the clinical picture, each common valvular lesion will be considered as being a pure uncomplicated process, the other valves being considered intact and functionating properly unless otherwise stated.

a. Aortic Disease. I. Insufficiency.

1. **Pathology.**—There may be sclerosis and deformity of the aortic valve, and this opening becomes larger than usual. The left ventricle is enormously dilated and hypertrophied. The papillary muscles are greatly flattened. The aorta shows an arteriosclerotic condition and other changes occur as other chambers are involved.

2. **Symptomatology.**—In the stage of compensation there may be headache, flashes of light, dizziness and faintness on arising quickly, palpitation and distress in the præcordium, pulsating arteries. In broken compensation the symptoms are dyspnœa, œdema, and possibly venous stasis

3. **Physiology.**—The headache and flashes of light are due to the disturbed flow of blood through the cerebrum; dizziness and fainting come from cerebral anæmia. The enormous size of the left ventricle, caused by regurgitation of the blood from the aorta results in a very strong, noticeable heart contraction. To this is due also the precordial distress and palpitation. The pulsating arteries are explained by partial emptying of the aorta into the ventricle during the diastole. Symptoms of broken compensation will be noted elsewhere.

Aortic Disease. II. Stenosis.

1. **Pathology.**—The pathology of aortic stenosis comprises a narrowing of the aortic valve; this either from cohesion of the segments, calcification, or exhuberant vegetation.

2. **Symptomatology and Physiology.**—The symptoms alone will in no case justify a positive diagnosis; dizziness and vertigo may occur from insufficient circulation in the brain, and signs of malnutrition may be present, since the heart may not be able to force an adequate amount of blood through the stenosed orifice.

In both the above lesions, mitral insufficiency may become a complication, when the symptoms enumerated below must also be considered possible.

b. Mitral Disease. I. Insufficiency.

1. **Pathology.**—There is usually an enlarged orifice, though there may be some stenosis; the valve segments may be shortened, and calcification may be very marked in cases complicating hypertrophy and dilatation of the ventricle; the ring may be dilated so the segments do not come into apposition. Dilatation and hypertrophy of both left

ventricle and right ventricle occurs in all cases, and hypertrophy of the right ventricle is a sequence.

2. **Symptomatology.**—In the stage of compensation there are no symptoms save a shortness of breath on exertion. The face may appear congested and other signs of insufficient circulation may appear. In time the compensation is broken and then dyspnœa, cyanosis, cough, venous stasis, and general dropsy may ensue.

3. **Physiology.**—The dilatation and hypertrophy of the left cavities is due to the regurgitation of blood from the ventricle at each systole. This overdistends the auricle and in addition congests the pulmonary circulation. The embarrassment of the pulmonary circulation is responsible for shortness of breath and dyspnœa and the cough which results from bronchial congestion. As compensation fails the heart is unable to stimulate the venous return flow, and there may be, in addition, pulmonic and tricuspid insufficiency, which adds to the venous stasis and lead to dropsy or effusion of serum into the tissues.

Mitral Disease. II. Stenosis.

1. **Pathology.**—Adhesion or calcification of the segments, causing a narrow orifice.

2. **Symptomatology and Physiology.**—There are no symptoms until compensation is broken; shortness of breath on exertion may exist, and a tendency to bronchitis may be marked. These are caused by pulmonary congestion due to increased intra-auricular pressure. When compensation fails, the pulmonic and tricuspid valves generally become incompetent and, as outlined above, venous stasis, dropsy, etc., ensue.

c. Disease of Pulmonary Valves.

1. **Pathology.**—The morbid processes involving the pulmonary valve segments are due most frequently to congenital malformation, stenosis being almost invariably due to this condition. Insufficiency, which lesion only will be considered here, frequently results from mitral disease. In addition to the insufficiency, dilatation and hypertrophy of the right ventricle exists.

2. **Symptomatology and Physiology.**—The dilatation and hypertrophy of the ventricle results from the increase in amount of work it must perform and increase in the fluid it must contain.

Other symptoms are those of broken compensation and have been discussed elsewhere.

d. Tricuspid Insufficiency.

1. **Pathology.**—There may be traces of endocarditis, but usually the insufficiency results from lesions of other valves; both right ventricle and auricle are dilated and hypertrophied.

2. **Symptomatology and Physiology.**—The symptoms are those of venous obstruction in the lesser circulation and venous stasis in the systemic circulation, and these symptoms have been outlined and explained previously.

5. DILATATION AND HYPERTROPHY.

In all the diseases previously considered and in arteriosclerosis there have been, in effect, conditions which called for an expenditure of heart energy greater than normal. Either adhesions or fibrous degeneration interfere with the normal activities of the heart muscle. Valvular diseases and chronic arteritis interfere with the normal current in the vascular channels. If such perversions of function occur, it is but natural to infer that in some way the heart muscle must adapt itself to changed conditions or the tissues would suffer from want of nutrition. That the heart muscle does adapt itself is shown by the fact that some of the most serious valvular lesions exist for long periods of time with no accompanying symptoms because the tissues are fully supplied with required nutrition. This fact may be explained theoretically by the following hypothesis: Every organ and tissue in the body is provided with a reserve power, that is, a latent ability for doing work which in health is not drawn upon except in case of some sudden strain. Now, in any lesion of the heart or vascular channels which requires more than the normal expenditure of muscle energy by the heart, this reserve is drawn upon, and if it is adequate to the demands made upon it no symptoms of failing circulation can be detected. If the increased demand on the heart occurs gradually and nutrition is good, there is built up an increased reserve power by hypertrophy of the muscular will and probable dilatation of the cavities. This condition may persist many years and the functional result be very gratifying. However, if the increased demands be sudden, or if nutrition of the heart wall be impaired, the normal reserve power is soon exhausted, no increased reserve can be built up, and dilatation with weakening and thinning of the heart walls ensues, resulting in symptoms of insufficiency or broken compensation. This only shows how serious lesions may exist.

1. **Pathology.**—The morbid conditions may exist in any of the cavities or walls of the heart. Irrespective of the endocardial and arterial changes which are considered elsewhere, we find, in a pure hypertrophy, no change in the size of the cavity or cavities of the heart, but a great increase in size and number of the muscle fibres. In dilatation with hypertrophy, the cavities are enlarged and the walls thickened. In dilatation with thinning, the cavities are enlarged and the walls thin.

2. **Symptomatology.**—In hypertrophy the symptoms are increased and forcible cardiac action, headache, epistaxis, facial congestion, and pulsating carotids.

In dilatation there is a weak, rapid pulse, dyspnœa, and symptoms of sluggish, obstructed venous circulation, as venous stasis, cyanosis, and even dropsy.

3. **Physiology.**—The increased and forcible heart action is due to the increased muscular power in the heart walls. The other symptoms are the sequelæ of the accompanying dilatation, since this increases the amount of blood thrown into the arteries by the powerful systolic contraction of the very strong walls of an enlarged cavity.

In incompensated dilatation the symptoms are explained upon this ground—viz., a weak heart must work rapidly to do its work at as well. If the cavity or cavities affected cannot empty completely and a constantly increasing residue accumulates, this causes acute dilatation, and if it is not relieved may result in complete failure of compensation, venous stasis, dropsy, etc.

Venous stasis results from failure of the heart to exert enough positive pressure to return the blood to the heart. Dyspnœa is caused by improper aeration of the blood in the congested lungs. Dropsy is the result of serous infiltration of the tissues.

6. ARTERITIS.

a. Acute.

Acute arteritis is an inflammation involving the coats of an artery.

1. **Pathology.**—Infiltration of the arterial coats with white blood cells and other exudative products, and, if nutrition is impaired, necrosis. The endothelium loses its normal lustre, becomes roughened, and thrombus formation is very probable.

2. **Symptomatology.**—There are no symptoms unless the thrombus occludes the lumen of the vessel, or is detached and carried as an embolus to some distant organ. The symptoms of such conditions have already been discussed and will not be repeated here.

b. Chronic.

While there are several forms of chronic arteritis, the following *résumé* is intended to convey a general impression of the condition known as arteriosclerosis.

1. **Pathology.**—Macroscopically the large vessels show yellow or whitish elevated patches which may soften or undergo atheromatous changes. The arterial walls are firm and unyielding and hard to compress. Microscopically, there may be infiltration and degeneration of the outer coats, and at these points the subendothelial

tissue begins a proliferating process to strengthen the otherwise weakened wall. It may degenerate or even break down or become calcified. The muscle fibres may be partially or completely degenerated.

2. **Symptomatology.**—Like most of the diseases of the circulatory system, while the heart is capable of responding to the increased amount of work required to pump blood through hard, unyielding arteries, arteriosclerosis is not productive of symptoms. When the heart dilates because of increased work, we have the symptoms of cardiac insufficiency which are outlined with dilatation.

In addition, there may be sudden death and gangrene of certain parts of the body.

3. **Physiology.**—Sudden death results from obliteration of the lumen of a coronary artery, either by an obliterating endarteritis, a thrombus, or an embolus. Gangrene of a limb is due to one of the same processes in an artery supplying it.

7. ANEURYSM.

Aneurysm is an enlargement along the course of a bloodvessel, caused by weakness or rupture of some of its coats. It is a frequent sequel of arteriosclerosis.

1. **Pathology.**—Dilatation of the lumen of the vessel, including all the coats; rupture of intima and distention of the other coats; rupture of media and sacculation of intima and adventitia through the rupture.

2. **Symptomatology and Physiology.**—The only symptoms are those due to pressure, and the location and size of the aneurysm determine what these symptoms shall be. For example, if the transverse arch is affected, cough and dysphagia may be caused by pressure on the trachea and œsophagus, the left recurrent laryngeal nerve may be so compressed as to cause paralysis of the left vocal cord, and pressure on the sympathetic ganglia may cause disturbances of the pupil. Erosion of the sternum or vertebræ may cause a continual gnawing ache, and so on. Within the scope of this work, it is impossible to take up more fully the different locations where aneurysms may occur, and the consequent symptoms, but a review of the organs and tissues which might be subjected to pressure by an aneurysm anywhere along the course of the large vessels will bring to mind, in a general way, the possible symptoms which would result from such pressure.

8. PHLEBITIS.

a. Acute.

1. **Pathology.**—Generally a pure phlebitis or inflammation around the vein extends into the vein wall and causes exudate of white and

red blood cells and fibrin into the different coats. If the intima affected, the endothelium becomes roughened, and upon the rou surfaces thrombi are very apt to form. Sometimes the process begi with the endothelium and involves the coats from within outward.

2. **Symptomatology and Physiology.**—There may be no sym toms aside from those of inflammatory reaction, but if the process extensive and accompanied by thrombosis, there may be gangrene the area from which blood is conveyed by the vein involved. If t thrombus is loosened or disintegrates, emboli in other parts of t body will occur.

b. Chronic.

1. **Pathology** comprises a thickening of the outer, inner, or all t coats of the vein wall. Syphilitic phlebitis may cause gummato or diffuse thickenings. Tuberculous phlebitis is characterized tubercle formation in the vein wall.

2. **Symptomatology and Physiology** are not marked unl thrombosis, embolus, or extensive occlusion occurs, where sympto are much as in acute type, but not so alarming. If the emboli a tuberculous, acute miliary tuberculosis results; characteristic milia tubercles forming wherever the bacilli are deposited by the blo stream.

CHAPTER IV.

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INTRODUCTION.

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3. LARYNGITIS.
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    b. CHRONIC.
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    b. CHRONIC.
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RESPIRATION.

INTRODUCTION.

RESPIRATION DEFINED AND CLASSIFIED.

FROM our studies in general physiology we know that that peculiar form of *energy* which we call *life* exists only in association with living cells or with living organisms, that it is liberated only through a katabolism or destructive metabolism of living cell protoplasm, and that this katabolism is possible in the presence of oxygen. The frequent use of such expressions as "*the spark of life*," "*the flame of life*," etc., indicates the analogy between the liberation of life energy and the liberation of the heat and light energy of fuel. It was once thought that these two processes were quite alike—each being a *combustion* or direct oxidation. The oxygen of the atmosphere unites directly with the carbon and hydrogen of the candle, of wood, of coal, or of illuminating gas to form CO_2 and H_2O—the process being attended with the liberation of energy; now the oxygen of the atmosphere forms combinations in the tissues and the combinations finally result in the formation of CO_2, H_2O, and CON_2H_4—the process being attended with the liberation of life energy. These two processes which seem so much alike are essentially different in a very important point. In the combustion of the hydrocarbons of the candle the affinity of oxygen for the carbon and hydrogen is so great that if once started the combustion proceeds by the invasion of the molecules by the oxygen, which breaks the bond between carbon and hydrogen and joins with each.

In the katabolism of the living protoplasm of the cell, the exceedingly complex protoplasmic molecule separates into two, perhaps more, simpler molecules; these simple molecules, which probably represent proteids, may again separate into still simpler ones. Each change from a complex to a more simple compound leads (I) to a liberation of energy, which may manifest itself in any of the activities of life, and (II) to a combination of simpler molecules with oxygen furnished by the cell sap or cell plasma. In the latter case, then the oxygen steps in to complete a molecule already nascent, while in the former case it is the *cause* of dissolution. To sum up the comparison: *Oxygen is the cause of combustion, but the complement of katabolism.* This general process of supplying the cells of a living organism with the requisite oxygen is called *Respiration.*

1. **Definition.**—Respiration is a general term which includes all of those activities involved in the furnishing of oxygen to the tissues of a living organism.

2. **Classification.**—The essential act of respiration is the taking up of oxygen by the living cell from the tissue plasma. In the large animals a more or less complex series of preliminary acts are necessary in order to furnish the tissue plasma with oxygen, and of this series of acts the interchange of gases between the blood and the medium surrounding the animal is the most prominent. This has led to the following classification: (I) Internal respiration, or cell respiration. (II) External respiration, or somatic respiration.

A. COMPARATIVE PHYSIOLOGY OF RESPIRATION.

a. Respiration by Individuals of the I, II, and III Order.

It has just been stated that the oxygen required in the cell at the moment of katabolism is furnished by the cell sap or cell plasma in which it is held in simple solution. If the cell is an independent organism—*e. g.*, an amœba, the oxygen of the cell plasma is immediately replenished from the water which surrounds the amœba. This is respiration in its simplest form. If the organism be an individual of the II or III order the process is essentially the same.

b. Respiration in Individuals of the IV Order.

1. **Cutaneous Respiration.**—The common earthworm or angleworm has well-developed, digestive, circulatory, nervous, reproductive and motor systems, but has no definite respiratory system. It has been found that the rich cutaneous capillary plexuses furnish to the blood an ample supply of oxygen, which finds its way easily through the delicate cuticle, attracted by the low oxygen pressure in

the cutaneous capillaries. In the amphibia the moist skin facilitates the diffusion of oxygen, and in this class of vertebrates cutaneous respiration is important, though always secondary to respiration by gills or lungs. A frog can live some time after the lungs have been removed.

2. **Respiration by Gills.**—Many invertebrates—*e. g.*, mollusca and aquatic arthropoda and all lower vertebrates, including tunicates, Enteropneusta, Amphioxus—and all fishes breathe by means of gills. A gill is an organ presenting numerous filamentous branches, whose delicate covering membrane affords slight resistance to the diffusion of oxygen into the blood from the water with which the gill is bathed.

3. **Respiration by Lungs.**—Most amphibians and all reptiles, birds, and mammals breathe atmospheric air into sac-like organs called lungs. The environment and habits of these animals necessitate the protection of the lungs within the body cavity. Here the blood in the capillaries is distributed over the surface of the minute air cells and the air, which has been warmed and freed from dust in its passage through the air channels, exchanges its oxygen easily through the thin, moist membranes of the air sac for the excess of CO_2 in the blood.

B. ANATOMIC INTRODUCTION.

The *skeletal features* particularly important in considering the physiology of respiration are summarized below under physiology of respiration because it contains matter not introduced into the anatomies, and intimately and indissolubly associated with the physiology of the mechanics of respiration.

For the same reasons the *muscles of respiration* are enumerated and classified under the mechanics of respiration.

The following additional facts of gross anatomy should be noted;

(*a*) **The Nasal Respiratory Passages** are tortuous, irregular in lumen, lined with a mucous membrane always well moistened with mucus, and provided, near the external opening, with numerous rather stiff hairs. The effect of this structure is to warm and free of dust the inspired air.

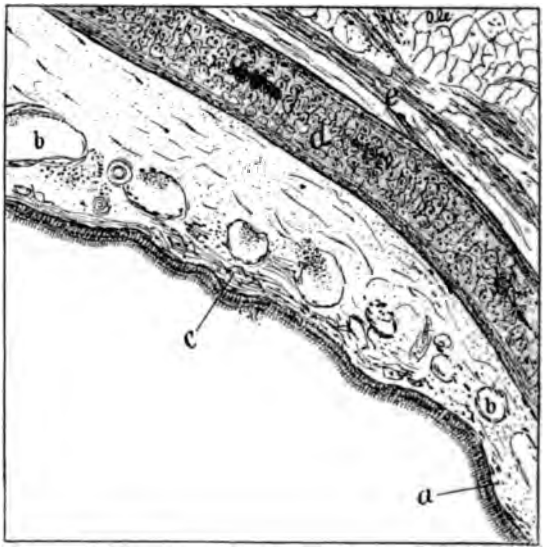
(*b*) **The Respiratoy Tract Crosses** the alimentary tract in the pharynx, a cavity common to both tracts. The respiratory passage is protected during the act of swallowing: (I) posteriorly by the epiglottis and the adduction of the vocal cords (for details see deglutition); (II) anteriorly by the elevation of the soft palate, and the elevation of the uvula. (See deglutition.)

(*c*) **The Trachea and Bronchi are Strengthened** and held open by heavy rings of cartilage. Thus protected the air passages remain open even when subjected to considerable pressure.

(*d*) **The Trachea and Bronchi are Lined** with a ciliated columnar epithelium, which is kept moistened with mucus secreted by the mucous glands of the submucosa as well as by goblet cells. The ciliary motion carries all secretions as well as particles of dust which pass the barriers in the nasal passages, upward toward the larynx from the deeper passages of the lungs. (See Figs. 114 and 115.)

(*e*) **The Trachea Branches** into two large bronchi, of which the left subdivides into two and the right into three subdivisions. The five branches subdivide dichotomously, until every lobule o the lung is supplied with a fine terminal bronchus which ends i

FIG. 114

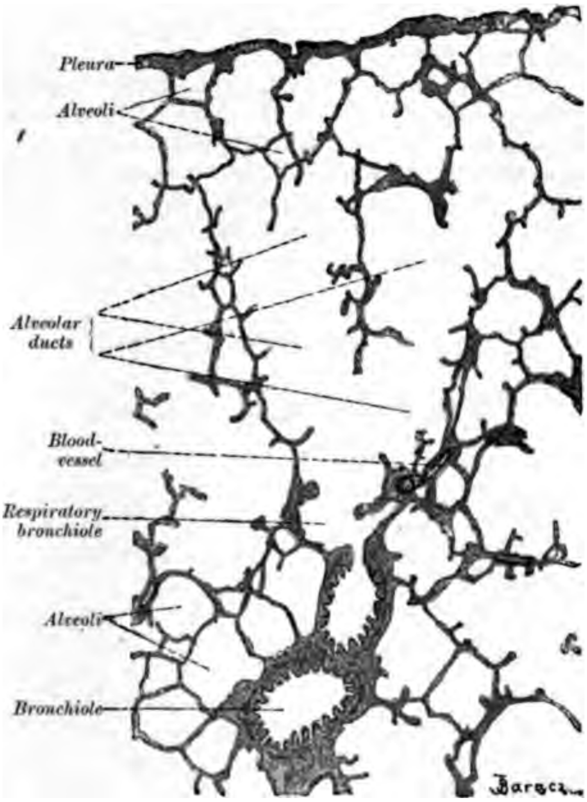


Section of a large bronchus: *a*, ciliated epithelium; *b b'*, small bloodvessels; *c*, muscularis mucosa; *d*, cartilaginous ring; *e*, muscle fibres surrounding cartilaginous ring.

delicate saccate air spaces or alveoli. "The part of the pulmonary parenchyma in communication with a single terminal bronchiole forms a pyramidal mass, whose apex corresponds to the terminal bronchus and whose base, when reaching the free surface of the lung, appears as one of the polygonal areas marking the exterior of the lung." (Piersol.)

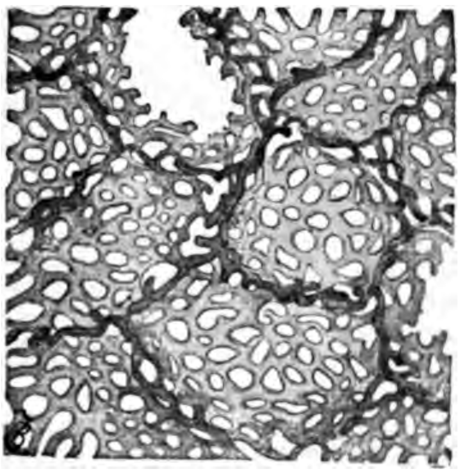
This pyramidal mass is called a *lobule*. Within the lobule the *terminal bronchus subdivides* into *two or three **alveolar ducts***, beset with air sacs, and the *alveolar ducts*, without subdivision, *open into or widen out into "blind," irregular, or **pyramidal*** spaces—the *infundibula*. The infundibulum is beset on all sides with air sacs

FIG. 115



Section of lung. (Szymonowicz.)

FIG. 116



Ideal section of lung, showing capillaries. (Szymonowicz.)

which open into the infundibulum, but do not communicate with each other.

(*f*) **The Impure Blood,** brought from the right heart by *the pulmonary artery,* is distributed to the lung tissue through branches which follow the subdivisions of the bronchi, finally reaching the lobule as an arteriole which subdivides into a network of fine capillaries lying in the walls of the alveoli or air sacs. The venous blood is thus brought into intimate relation with the atmospheric air which enters the alveoli. Fig. 116 shows the capillary network which surrounds the alveoli.

C. PHYSICAL INTRODUCTION.

The Solution of Gases in Liquids.

If one were to place a litre of hydrant water under the receiver of an air pump, he would find that the water subjected to a vacuum would give off gas vigorously, the quantity depending upon the conditions which had existed before the experiment. An analysis of this gas would show it to be nitrogen, oxygen, and carbon dioxide, or the same gases to which the water had been exposed in its contact with the air. If we expose H_2O to an atmosphere of HCl gas it will rapidly absorb large quantities, forming the common hydrochloric acid. So it becomes evident that water may hold considerable quantities of gases in solution. Just how much gas any liquid will absorb depends upon the nature of the gas and the nature of the liquid; but the amount of any particular gas which a particular liquid will absorb varies with the pressure of the gas in the atmosphere to which the liquid is subjected. For example, if the amount of oxygen in the air were doubled, water would absorb twice as much; but if it were reduced to one-half or one-third of its present proportion, water would absorb proportionately less. Any change in the proportion in the air is quickly responded to by a readjustment of the proportion in the water through simple diffusion, to again reach an equilibrium.

The following laws have been formulated by McGregor Robertson (*Physiological Physics*, p. 291):

(I) THE GASES MOST READILY LIQUEFIED ARE THOSE WHICH ARE ABSORBED IN THE GREATEST AMOUNT.—CO_2, NH_3, and HCl are at once most easily liquefied and absorbed. Oxygen, nitrogen, and hydrogen are liquefied with difficulty and are feebly absorbed.

(II) DIFFERENT LIQUIDS ABSORB DIFFERENT QUANTITIES OF THE SAME GAS.—The *coefficient* of *absorption* (*a*) or the solubility of a gas is the volume of gas absorbed by a unit volume of the liquid at 0° C. and 760 mm. Note that (*a*) is determined for ***constant temper-***

ture and pressure. The coefficient of absorption of O, CO_2, and N n water is 0.05, 1.8, and 0.0235, respectively.

(III) The Amount of Gas Absorbed by the Same Liquid Varies with the Temperature.—The higher the temperature the smaller he amount of gas which may be held in solution, and conversely. Heating a liquid drives off much of the dissolved gas. One volume of H_2O at 15° C. and 760 mm. pressure absorbs, of oxygen, 0.034; of carbon dioxide, 1.002; of nitrogen, 0.017 volumes.

(IV) The Amount of Gas Absorbed by the Same Liquid Varies with the Pressure.—The higher the pressure of the gas above he liquid the greater the amount which will be dissolved by the iquid. If the pressure be relieved, as in the opening of a bottle of "soda-water," the gas (CO_2) escapes rapidly with effervescence. One volume of H_2O at 0° C. and $\frac{760\ mm.}{2}$ pressure will absorb of oxygen $\frac{0.0489}{2} = 0.0245.$

(V) The Absorptive Power of a Liquid for a Particular Gas is Independent of Other Gases which it May Already Hold in Solution.—Thus a liquid in contact with a mixture of gases absorbs a quantity of each gas, just as if it were the only one present, the amount being determined by the coefficient of absorption and the pressure of the gas in the mixture, or the Partial Pressure.

(VI) Each Gas Forming a Part of a Mechanical Mixture Exerts a Partial Pressure Proportional to its Part of the Mixture.—Taking the proportions of the gases in the atmosphere, one concludes that as oxygen represents 20.96 per cent. (say 21 per cent.) of the mechanical mixture, its partial pressure would be 21 per cent. of the whole pressure—*i. e.*, 21 per cent. of 760 mm. mercury or atmospheric pressure. Partial pressure for oxygen in pure air is 0.21 × 760 = 158 mm. mercury. Partial pressure for CO_2 in pure air is 0.0004 × 760 = 0.3 mm. mercury. It is estimated that in the alveoli of the lungs the partial pressure for oxygen is 122 mm.; for CO_2, 38 mm.

The absorption of oxygen at 37.5° C. and partial pressure of the alveoli, or 16 per cent. of 760 mm. $a = 0.026 \times \frac{16}{100} = 0.004 +$, *i. e., blood plasma at body temperature would absorb from the alveoli of the lungs* 4 *c.c. oxygen for every litre of plasma.* If absorption of oxygen were to depend solely upon its physical relation to plasma this would be practically the limit of absorption.

The absorption of CO_2 at 37.5° C. the partial pressure of CO_2 n the alveoli being 5 per cent. of 760 mm. $a = 0.569 \times \frac{5}{100} = 0.028 +$, *i. e.*, if in the alveoli of the lungs the atmosphere contains 5 per cent. of CO_2, 100 volumes of plasma would absorb 2.8 volumes of CO_2; or, in other words, CO_2 can, according to this course of reasoning, be diffused from the blood into the air passages only when the amount in the plasma exceeds 2.8 c.c. per 100 c.c. plasma. Furthermore, that this proportion would represent approximately the proportion of CO_2 in arterial blood, as far as it could exist under physical laws.

THE PHYSIOLOGY OF RESPIRATION.

A. THE MECHANICAL AND PHYSICAL FEATURES OF RESPIRATION.

1. THE STRUCTURAL FEATURES.

If the constituents of the atmosphere were compelled to make their way through the respiratory passages by simple diffusion, the amount of oxygen received into the blood would at best permit a most sluggish katabolism. It may have been observed that the *frog* uses the floor of the mouth as a sort of bellows to pump air into the lungs, while an occasional spasmodic contraction of the body wall forces the air out. *In birds* the elastic bony thorax is compressed by muscles of the body walls; this action forces the air out of the lungs. Relaxation of the abdominal muscles allows the thorax to regain its original volume and air rushes in to fill the lungs. *In mammals* the condition is quite opposite, the inspiration representing the muscle contraction and the expiration representing relaxation.

The anatomic characters of the mammalian thoracic skeleton, which are of especial importance physiologically, are: (I) The *mobility* of the posterior greater than that of the anterior part of the thoracic skeleton. (II) The *posterior slant* of the ribs. (III) The *double vertebral attachment* of the ribs, making an axis of rotation which does not coincide with the axis determined by the simple raising and lowering of the ends of the ribs. (IV) The noticeable angle which the fourth, fifth and sixth ribs make with their cartilages. (V) More important than any skeletal character is the fact that the thoracic cavity is separated from the abdominal cavity by a *muscular partition* which is very convex upward or anteriorly. When the radial muscle fibres of this *diaphragm* contract the arch is flattened, the contents of the abdomen pressed farther downward, the capacity of the thorax suddenly increased: but any increase in the capacity of the thorax must lead to a rarefaction of the air, or to negative pressure. This tendency to the production of negative pressure is speedily satisfied by the influx of air through the respiratory passages filling the lungs, which in turn fill the increased space of the thorax. Through the action of the diaphragm, then, the anteroposterior dimension of the thorax is increased.

a. The Changes of the Thoracic Diameters.

(*a*) **The Anteroposterior Diameter** is actively increased by the contraction of the diaphragm and passively decreased by the relaxation of the diaphragm. It may be actively decreased by a contraction of the abdominal muscles, which forces the contents of the abdomen up against the diaphragm, distending its arch, thus further encroaching upon the thoracic cavity and forcing air out of the lungs.

(*b*) **The Dorsoventral Diameter** is increased by the contraction of the external intercostal muscles. The mechanism of the movement is as follows: (I) ribs more and more mobile from before backward; (II) ribs slant posteriorly; (III) external intercostals, having their origin on the posterior margin of a rib, pass ventrally and posteriorly to be inserted upon the anterior margin of the next succeeding rib. With all of these peculiarities of structure a contraction of the external intercostals must result in an elevation of the ends of the ribs and a carrying of the sternum farther away from the vertebral column. Still another factor in this is the opening of the angle between the fourth, fifth, and sixth costal cartilages and their ribs. The dorsoventral dimension is decreased by the elasticity of the thorax, which causes it to return to its former size on relaxation of the external intercostals.

(*c*) **The Lateral Diameter.**—By virtue of the double vertebral attachment of the ribs, mentioned above, the action of the external intercostals is not only to carry the end of a rib farther from the vertebral column as its general line approaches a position perpendicular to the spine, but also to carry the middle of the rib farther from the median line of the thorax as the plane, which its curve determines, approaches the perpendicular to that tine. It might at first be supposed that a contraction of the diaphragm would pull in the walls of the thorax, thus decreasing the lateral dimensions; but Brücke showed conclusively that though it undoubtedly exerts a strong tension on the thoracic wall the high-domed mass of abdominal viscera, upon which the force of the diaphragm is directly exerted, is pressed downward and outward against the upper abdominal walls and so neutralizes the tendency in the opposite direction.

b. The Muscles of Respiration.

1. **Muscles of Quiet Respiration.** (*a*) **Inspiration.**—(I) *The diaphragm;* (II) the M. levatores costarum longus et brevis; (III) Mm. *intercostales externi* et intercartilaginei.

(*b*) **Expiration.**—*Ordinary quiet expiration is non-muscular,* depending upon the weight and elasticity of the tissues. Inspiration throws the tissues out of the position of rest and they fall or sink back to that position during expiration.

2. **Muscles of Forced Respiration.** (*a*) **Inspiration.**—Besides those of quiet respiration the following: (*α*) *Upper ribs raised by:* (I) the three M. scaleni; (II) M. serratus post. superioris; (III) M. cervicalis ascendens. (*β*) *Sternum is raised by:* (IV) Musculus sternocleidomastoideus; (V) M. sternohyoideus; (VI) M. sternothyroideus; (VII) M. thyrohyoideus. (*γ*) *The hyoid bone is raised by:* (VIII) M. mylohyoideus; (IX) M. stylohyoideus; (X) M. geniohyoideus; (XI) M. digastricus. (*δ*) *The shoulder girdle is raised and drawn backward by:* (XII) M. trapezius; (XIII) Mm. rhomboidei, major, et minor; (XIV) M. levatores anguli scapuli. (*ε*) *Lower ribs drawn toward the raised and fixed upper ribs by:* (XV) Pectoralis major et minor; (XVI) subclavius; (XVII) serratus magnus.

(*b*) **Expiration.**—(*α*) *Abdominal contents compressed and forced against diaphragm by:* (I) M. obliquus externus; (II) M. obliquus internus; (III) M. transversus abdominis; (IV) M. rectus abdominis; (V) M. levator ani. (*β*) *Ribs are depressed by:* (VI) Intercostales interni; (VII) M. rectus abdominis; (VIII) M. quadratus lumborum; (IX) M. serratus posticus inferior; (X) M. triangularis sterni.

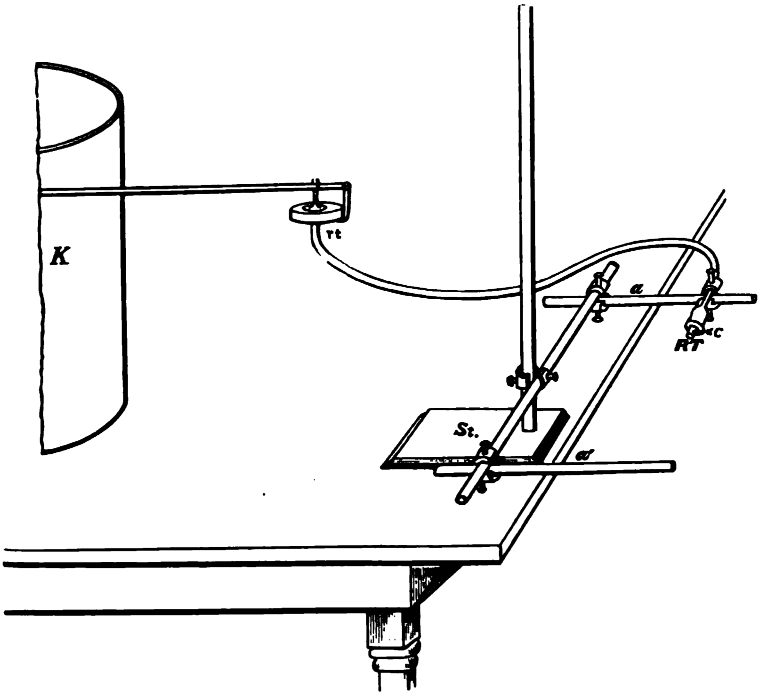
2. OBSERVATION OF CHANGES IN THE DIAMETER OF THE THORAX.

The *observations* of the *dorsoventral* and the *lateral diameter* are usually taken in the plane of the nipples or in the plane of the junction of the ninth rib with its costal cartilage. These thoracic planes must be taken perpendicular to the axis of the thorax.

1. **The Calipers.**—This instrument is a most reliable apparatus for determining the diameter. As usually constructed, a graduated arc near the hinge of the instrument enables one to read off at once the number of centimetres between the points of the two limbs of the instrument. One may measure the dorsoventral or the lateral diameter of the thorax when the thorax is in repose, or at the end of forced inspiration or of forced expiration. Such observations give not only the actual diameters, but the amount of expansion of the chest during the respiratory movements.

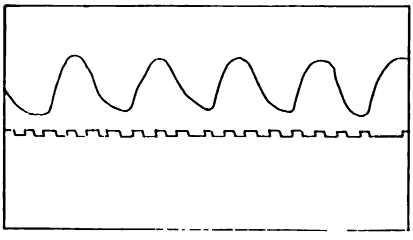
2. **The Stethograph.**—The accompanying figure (Fig. 117) shows convenient form of this instrument. As the name suggests, the

FIG. 117



he human stethograph : *St*, stand with heavy base, supporting a thoracic frame, constructed as-pipes and clamps ; *a* and *a'*, horizontal parallel arms, to be adjusted on either side of the rax ; *a'*, to touch the thoracic wall ; *R T*, receiving tambour, constructed as described in the endix ; the movements of the cork *c*, which touches the thoracic wall, are transmitted to recording tambour *rt*, thence traced on the kymograph *K*.

FIG. 118

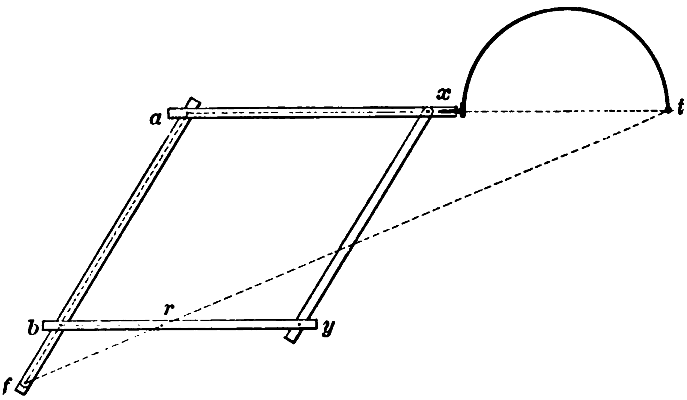


Normal stethogram of dorsoventral diameter in nipple plane.

rpose of this instrument is to record the movements of the chest. course is had to a pair of Marey tambours. The button (*c*) of the receiving tambour (*R T*) follows the movements of the chest wall; the changes of the pressure in the receiving tambour are communicated through a rubber tube, and the record is received upon carboned paper. Fig. 118 gives a normal stethogram. Note (I) that the rise (inspiration) is more rapid than the fall (expiration); (II) that both inspiration and expiration are more rapid at first and gradually slow off at the end of the act; (III) that there is a moment between the acts when there seems to be no movement at all; (IV) that this moment of perfect inactivity is longer at the end of expiration than at the end of inspiration.

3. **The Chest Pantograph.**—This instrument, in tracing upon "millimetre" or "ordinate" paper an outline of the thorax at any

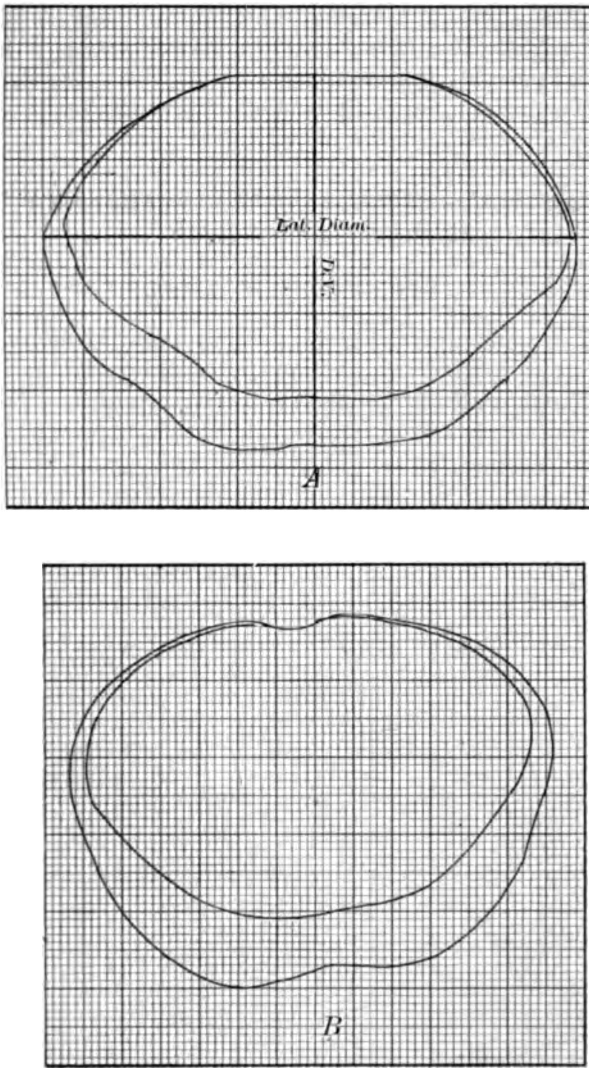
FIG. 119



The chest pantograph, for measuring and recording chest contours. The instrument is co structed of brass or of wood, with brass or steel semicircle. The joints *a*, *b*, *x*, and *y* mo easily in the plane of the instrument. The semicircle, 40 in. in diameter, rotates at *x* arou the diameter *t x*. The point *f* is fixed to a table. With *f* a fixed point, all movements of *t*, t tracing point, are accompanied by corresponding movements of *r*, the recording point. Th triangles *f r b* and *f t a* are similar triangles in all positions of the instrument $fb : fa :: fr : ft$ but $\frac{fb}{fa} = \frac{1}{5}$; therefore, the distance *fr* is always $^1/_5$ the distance *ft*.

level, enables one to determine quantitatively not only any diameter, but the area also, as well as any peculiarities of sectional contour. Just this feature of the instrument enables it to do what the other appliances above described fail to do. For description of this instrument see explanation of Fig. 119. If the subject to be examined sit beside a table on which the instrument is fixed; if the seat be adjusted in height to bring the plane of the thorax to be examined into the plane of the instrument—*i. e.*, on a level with the top of the table; if a sheet of millimetre paper be fixed to the table under the recording pencil *r;* and if the tracing point *t* be swept around the thoracic wall, a record of the chest contour will be traced upon the paper. The accompanying Fig. 120 shows two such contours from hy, well-developed young men. Two millimetres in the figure l one centimetre of actual measurement. The inner contour

FIG. 120



Contours of chest, taken with chest pantograph.

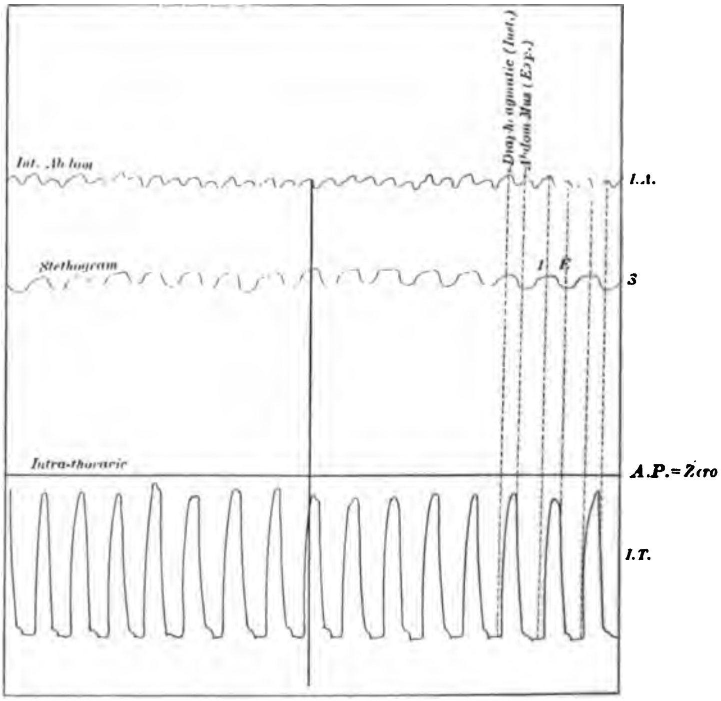
at of forced expiration, while the outer one is that of forced ation. In contour A the increase of lateral diameter by forced inspiration is 2 cm., while the increase of dorsoventral is 3 cm. In the same contour the cross-sectional area of the thorax in the plane of the ninth rib is represented by 25.52 of the larger squares containing 25 square cm.; total area = 637.5 square cm., while the cross-sectional area of the chest in forced expiration is 517.5 square cm. Forced inspiration shows an increase of 120 square cm., or about 23 per cent. over the cross-sectional area of forced expiration. Furthermore, both coutours show a prominence on the right side (left in the figure), probably due to stronger musculature on that side

3. THE PHYSICAL EFFECTS OF THE CHANGES OF THE THORACIC DIMENSIONS.

a. Intrathoracic Pressure.

Intrathoracic pressure is the pressure in the thoracic cavity outside of the air passages—that is, in the pleural and mediastinal cavities especially, though it affects the blood and lymph vessels of the thorax

FIG. 121

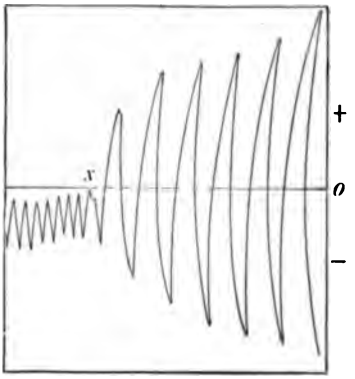


Simultaneous tracings of intrathoracic pressure (*I. T.*), intra-abdominal pressure (*I.A.*), and a stethogram (*S*); *A.P.*, atmospheric pressure equals zero.

are not in either of the two cavities mentioned. If one introduce
he pleural cavity or the mediastinal cavity a cannula whose
al end communicates through a tube with a recording tambour
h a manometer, it will be found that there is a fall of the record-
ver or of the mercury, indicating a fall of pressure below the
pheric pressure. In fact, the recording lever or the mercury
ot again rise to the level of atmospheric pressure: but will
te up and down below the zero line, being lower during inspira-
ian during expiration. Fig. 121 gives a tracing of intrathoracic
ire (*I. T.*), atmospheric pressure (*A. P.*), intra-abdominal
ire (*I. A.*), and a stethogram (*S.*). The tracings were taken
a rabbit under ether, and are simultaneous. The thing which
be first established is the relation between the intrathoracic
ire and the respiratory movements. When the chest wall rises in
ation—tracing *S*, phase *I*—note that the thoracic pressure falls
minimum; when the chest wall falls in expiration (*S–E*) the
ioracic pressure reaches a maximum. This maximum does not
the zero-line under ordinary circumstances—that is, *intrathoracic*
re is always negative, but it is more negative during inspiration
luring expiration. If the lungs were inelastic sacs the pressure
en the lungs and the thoracic wall—intrathoracic pressure—
become zero almost instantly on the cessation of the inspiratory
But while the thoracic wall is by its elasticity regaining its
al position of repose at the end of expiration the elastic sacs
the thorax are contracting by
of their elasticity. Now, inas-
as the elasticity of the lungs
be overcome by the negative
ire outside of them, it is easy to
at when there is no obstruction
exit of air from the lungs they
end to assume their position of
more quickly than will the
ic wall—that is, they will tend
ll away from the thoracic wall,
g a negative pressure in the
l cavity.

athoracic pressure may be posi-
there is a forced expiration
occluded exit of air; or in a
expiration with a partial ob-
ion to the free exit of air the
ire in the pleural cavity will be positive. In Fig. 122 the nostrils
rabbit under observation were held shut at *x*. The vigorous
atory acts which the animal made in its effort to get air made
spiratory pressure much lower than usual and the expiratory

FIG. 122



Tracing of intrathoracic pressure showing influence of an obstruction in the air passages introduced at *X*.

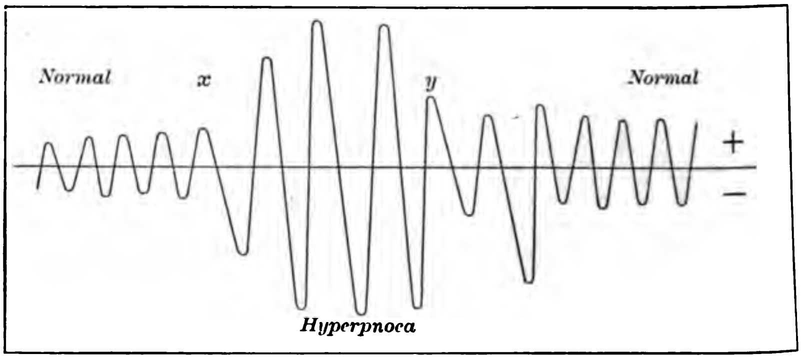
pressure much higher than usual, reaching almost as far on the positive side of the zero line as on the negative side.

Physiologically the intrathoracic pressure is positive during the forced expiration of coughing, sneezing, and straining at stool, or lifting. The face becomes red in the two last because the positive pressure is sustained, blocking venous flow to the heart.

b. Respiratory Pressure.

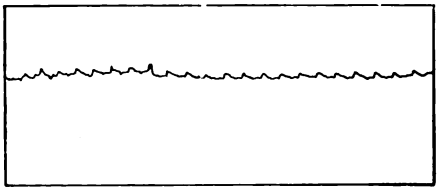
Respiratory pressure is the pressure in the air passages. It is always negative during inspiration and always positive during expiration. If it were not negative during inspiration the air would not flow into the lungs, and if it were not positive it would not flow out of the lungs during expiration. In quiet breathing the respiratory pressure is only slightly positive and slightly negative. Should the air passages become partially obstructed, as in sneezing or coughing, the positive pressure of expiration may be very high. During lifting or straining at stool the positive pressure in the air passages exceeds

FIG. 123



Tracing showing respiratory pressure as recorded by tambours. At *x* the nostrils of the animal were held closed ; at *y* they were released.

FIG. 124



A cardiopneumatogram, showing influence of the pulsation of the thoracic arteries upon air in the respiratory passages. The respiratory movements were suspended.

he positive pressure in the pleura by the amount of the elasticity of he lungs. If one hold in the mouth or nose a tube whose distal end s connected with a recording tambour, one will notice that the ecording lever rises and falls synchronously with ventricular systole, r with the pulsations of the thoracic arteries. To trace this "cardio-neumatogram" one must either breathe very quietly or suspend espiration altogether for short periods, during which the tracing may e taken. Note in the accompanying tracings indubitable evidence of ystolic and dicrotic pulse waves which have been transmitted through he air of the respiratory passages and thence to the recording lever *ia* the tambour and tube. (See Fig. 124.)

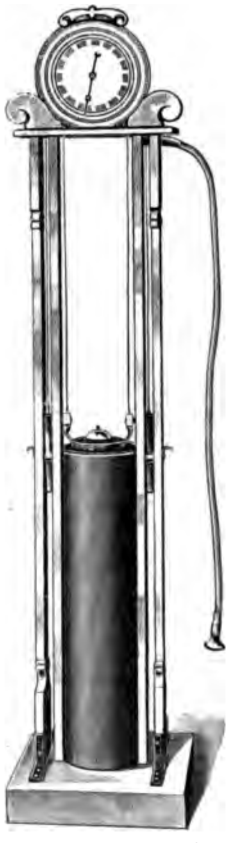
c. Intra-abdominal Pressure.

Intra-abdominal pressure is zero or very near zero at the end of xpiration in quiet breathing—that is, when thoracic and abdominal walls are in a state of perfect repose. When the diaphragm descends n inspiration the pressure becomes decidedly positive, forcing abdominal viscera and wall outward against atmospheric pressure. See Fig. 121, *I. A.*) If the viscera and wall regain their position of epose in response to the elasticity of the abdominal wall there will e but one wave of positive pressure and that is caused by the descent f the diaphragm. It occurs when intrathoracic pressure is lowest. f there is an active contraction of abdominal muscles—as in the ase in Fig. 121—there will be a second rise of pressure due to that ontraction, and it will occur during expiration. These relations are well shown in the tracing. The influence of intra-abdominal pressure upon venous and lymphatic circulation has been discussed above. oughing and sneezing cause a sudden positive pressure of moderate degree, but straining at stool, lifting, and straining in parturition ause a sustained positive pressure of high degree, and a consequent orcing of blood and lymph already in large abdominal vessels into he thorax, but a blocking of any further entrance of venous blood r of lymph into the abdomen, thus backing it up in the veins of he lower extremities.

d. Lung Capacity.

This expression is used to indicate the quantity of air flowing nto or out of the lungs during respiration. The instrument used o measure the air is called a *Spirometer.* If the air is collected over water it is a *Wet Spirometer* (see Fig. 125); if in an elastic bag, a *Dry Spirometer.* The results obtained from observations will vary within wide limits and according to the combination of several factors —*e. g.*, stature, girth of chest, muscular development, habits, age, sex, accumulation of fat, etc. If an average-sized man, of average muscular development, breathe quietly into a spirometer it will be observed that only 300 to 500 c.c. flow into and out of the instrument with each respiration. This quantity of air involved in normal quiet respiration is called TIDAL AIR. The quantity will vary from 300 c.c. in perfect rest to 500 c.c. or more during or just after moderate exercise, as in walking.

FIG. 125



The water spirometer. The outer receptacle contains water. The inner, inverted reservoir receives air through the mouth tube at the right, and is raised.

But if the exercise be more than the most moderate, the respirations will deepen until the tidal air may reach 1000 c.c., or even more. If 500 c.c. be arbitrarily assumed as tidal air, then the excess which may be inspired in forced inspiration is called COMPLEMENTAL AIR, and for men of average stature and development this will approximate 1600 c.c. If at the end of such a forced inspiration an expiration is begun which empties out the 1600 c.c. and the 500 c.c., it will be found that the muscles of forced expiration can force out still more air to the extent of another 1600 c.c. This last air of forced expiration is called RESERVE AIR. The total quantity expired after forced inspiration is called VITAL CAPACITY and is the sum of the tidal, complemental, and reserve (500 + 1600 + 1600 = 3700 c.c.). But at the end of forced expiration the lungs are not empty. There still remains a so-called RESIDUAL QUANTITY, which is estimated at 1600 c.c. It is an accidental forcing out of a part of this residual air that causes such inconvenience when one gets a forcible and unexpected thump on the thorax.

A diagram representing these terms and definitions will be found in Fig. 126.

c. Types of Respiration.

1. Diaphragmatic, Inferior Costal and Superior Costal Types.—An infant breathes almost exclusively by means of contractions of the diaphragm. The flattening of the arch of the diaphragm presses upon the abdominal viscera and pushes out the abdominal walls; this type of respiration is called *abdominal* or *diaphragmatic.* At about the age of puberty there is, in all European races at least, a distinct difference in the male and female respiratory movements.

The Cheyne-Stokes Type of Respiration.—The accompany- igure, Fig. 127, represents a stethogram with a slowly rotating . Note the series of rather rapid, deep respiratory movements iating with perfect rest in the recorded case above. Sometimes, ver, there is an alternation of a series of deep with a series of ›w respirations. In the latter form it is frequently to be noticed ildren during sleep. It is seen in chloral poisoning, morphine

FIG. 126

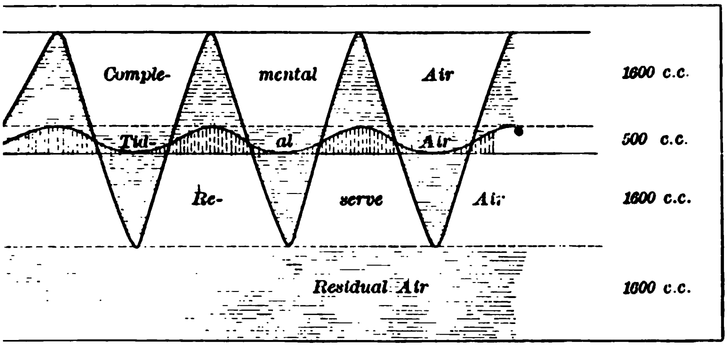
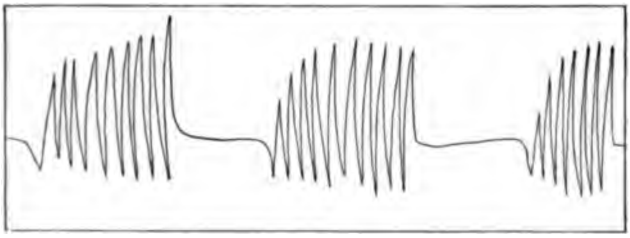


Diagram of lung capacity.

ning, and in nervous diseases which interfere with the action : centre. The Cheyne-Stokes respiration in its physiologic forms s to bear to respiration a relation analogous to that which the be-Hering pressure curves bear to circulation; both rhythms iate in the medullary centres, the first governing respiratory

FIG. 127



Cheyne-Stokes respiration.

m and the second governing vasoconstrictor tonus. The cycle ie Cheyne-Stokes movements is repeated once to three times ninute.

the male the ventral line is somewhat farther advanced in the r costal and abdominal regions than is the case in the female, : in the female the upper costal region is advanced relatively er. These two types are called respectively the inferior costal and superior costal type. Note that in deep inspiration, shown in the interrupted line, the inferior costal type of the male is more pronounced—*i. e.*, in deep inspiration the ninth rib girth expands most in the male, while it is the girth in the nipple plane which expands most in the female. There has been some controversy as to the reason for this difference. Is it fundamental or incidental? Is it due to sexual life—viz., childbearing in the female? If so, all women of all races should show it. Some authorities (Mays and Kellogg) say that the American Indian women and Chinese women do not show the superior costal type of breathing, and, therefore, the difference must be incidental and probably depends upon dress.

f. Modifications of the Respiratory Act.

1. **Coughing.**—When the respiratory mucous membrane, in or below the larynx, is irritated by inhaled dust or gases or by exuded secretions—mucus or mucopus—the system makes an effort to expel the offending substance by a forcible expiration accompanied by a closure of the larynx followed by its sudden opening and an explosive expulsion of the air in the upper air passages. This blast of air usually carries with it the irritating matter.

2. **Sneezing.**—When the nasal mucous membrane is irritated in any way a similar expulsion of the air through the nose serves to remove the irritating matter. Both coughing and sneezing are preceded by an inspiration of more than usual depth.

3. **Yawning.**—If for any reason the respiration has fallen behind the requirements of the system for oxygen there is an involuntary effort on the part of the respiratory system to make the deficiency good. This is accomplished through a prolonged and very deep inspiration, followed by a very complete expiration, and this in turn followed by a rather deep inspiration, after which the respiration proceeds in the usual quiet rhythm.

4. **Hiccoughing.**—Hiccough consists in a sudden contraction of the diaphragm which causes a spasmodic inspiration; this is blocked by the sudden closure of the glottis, causing the characteristic sound. Hiccough may be caused by certain kinds of gastric irritation, especially the taking of dry food or the mechanical irritation which the stomach undergoes incident to inordinate laughing, where it is subjected to a series of quick pressures by the abdominal muscles. In the first case a drink of water usually stops the hiccough: in any case it is likely to stop if the attention is either closely fixed upon it or completely diverted from it.

5. **Sighing.**—Sighing is very similar to yawning in its mechanism, except that its cause is due primarily to the emotions. Grief, sorrow, and even extreme fatigue may be accompanied by sighing.

6. **Crying and Laughing.**—These are purely emotional in their origin and consist of a deep inspiration (in crying) usually followed

by a series of spasmodic vocalized expirations (in laughing usually). Crying and laughing are subject to so many individual peculiarities in sound and in facial expression that it is impossible to draw a distinct picture of either or a definite line between them.

7. **Sobbing.**—After prolonged crying the respiration is likely to take the form of sobbing which is a series of convulsive inspirations accompanied by partial closure of the glottis.

B. THE CHEMISTRY OF RESPIRATION.

1. EXTERNAL RESPIRATION.

a. Respiratory Changes in the Air Breathed.

1. **Composition of the Normal Atmosphere.**—The open atmosphere is a mixture of gases in the following approximate proportions:

Atmosphere	Nitrogen, including argon, etc.	79.00	in 100 parts.
	Oxygen	20.96	
	Carbon dioxide	0.04	
	NH_3, H_2O; organic matter, in small variable quantities.		

Though the quantity of H_2O in the air is considerable—over 1 per cent.—it is not customary to reckon it in with the gaseous constituents. How is the air changed during its stay in the lungs? An apparatus may be constructed which will show both qualitatively and quantitatively the principal changes effected. If a small animal be confined in a sealed chamber and provided with dried air which has been deprived of all CO_2 it will be found that the air on leaving the chamber has received considerable CO_2 and H_2O and a small amount of organic matter, and that it has a higher temperature. Systematically enumerated, the changes in respiration are:

2. **Qualitative Changes Produced by Respiration.** (*a*) **Change of Temperature.**—Air below 36° C. would always be increased in temperature, though not quite to blood temperature, 38° C. In ordinary quiet respiration of air at ordinary room temperature (20° C.) the expired air has a temperature between 36° C. and 37° C. Very cold air would not be raised to that temperature, and very warm air (40° C.) would not be lowered to that temperature.

(*b*) **Change in Proportion of CO_2.**—The CO_2 is always increased. If the inspired air be pure the expired air will contain 4 per cent. to 5 per cent. (4.34 per cent.) CO_2.

(*c*) **Change in Proportion of Oxygen.**—The oxygen is always decreased. If the inspired air be pure—*i. e.*, has 20.96 per cent. oxygen—one-fourth of the oxygen is consumed at one breathing of the air. With successive re-breathing less and less oxygen is consumed, but eventually it can all be taken out of the air, leaving the latter quite free of oxygen and composed of 79 per cent. of nitrogen; CO_2, H_2O, etc., 21 per cent.

(*d*) **Change in Volume.**—If the volume of inspired air be compared with that of the expired air it will be found that it is greater; but we must not forget that the expired air has a higher temperature, and that increase in temperature makes a marked difference in the volume of gases. If we reduce it to the same temperature it will be found to have actually decreased slightly in volume. Now, one litre of oxygen, combined with carbon, makes one litre of carbon dioxide at the same temperature and pressure. If the oxygen of the inspired air has all combined with carbon, why should there be any decrease in volume? But the oxygen of the inspired air does not all combine with the carbon; some of it combines with hydrogen to form H_2O, and that causes the difference in volume.

(*e*) **Change in the Proportion of Water.**—The water is generally increased, though it may be decreased. Though the cool inspired air may be saturated with water at that temperature, the raising of the temperature in the air passages increases the capacity of the air for water and more is taken up from the moist mucous membrane. If warm air is saturated with moisture before entering the lungs it will take up very little more. If warm air be dry—the usual condition in furnace-heated houses—it will take up moisture very rapidly from the nasal passages and trachea and upper bronchi. This is irritating to the delicate membranes and is one of the many causes for catarrh.

(*f*) **Organic Matter** in minute quantities is added to the air in the lungs.

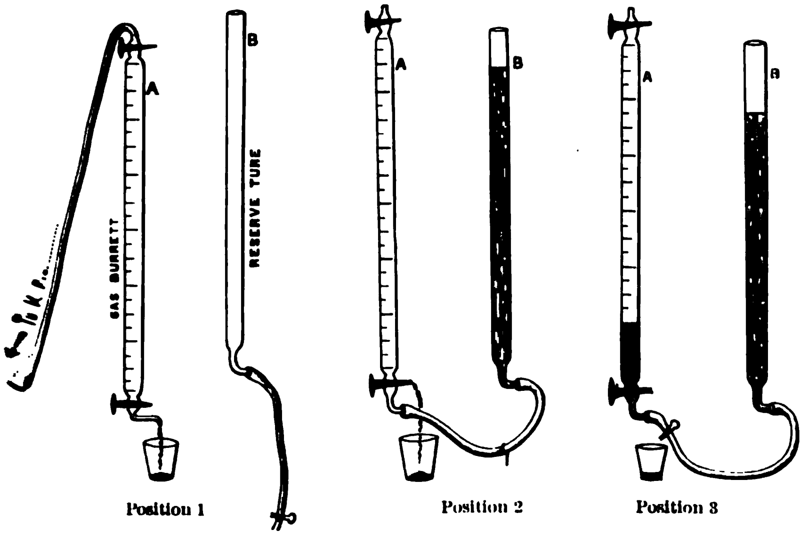
3. **Quantitative Changes of the Air in Respiration.** (*a*) **The Estimation of the Oxygen in Expired Air.**—The accompanying Fig. 128 shows a very efficient and simple appliance for the determination in question. The expired air analyzed should represent the well-mixed product of many expirations. This may be accomplished by inspiring from the open atmosphere and expiring into a spirometer or similar receptacle. After sufficient time has elapsed for complete diffusion of the gases and cooling to room temperature, 100 c.c. may be drawn off and analyzed. Finally a correction must be made for temperature and pressure and all corrected readings given for 0° C. and 760 mm. pressure. The quantity of oxygen in the open atmosphere may be determined as a preliminary step in the experiment.

The oxygen is determined by a volumetric method, using two or more gas burettes and a solution of potassium pyrogallate. The solution of potassium pyrogallate is prepared by mixing two parts of 25 per cent. aqueous solution of KOH and one part of 5 per cent. aqueous solution of pyrogallic acid..

These two constituents of the pyrogallate should be mixed in the pressure tube of the gas apparatus just before the analysis is made.

To collect samples of air for analysis, one fills the gas burette (Fig. 128, *A*) with water by suction. Connection is then made between the exit tube at *k* (of the respiration apparatus used in the previous experiment) (see Fig. 128) and the upper end of the gas burette as shown in Fig. 128, position 1, the respired air flows in, displacing the water. The stopcocks are now turned so that no air can escape from the burette. The rubber tube of the pressure tube (*B*), which has been filled with the potassium pyrogallate, is now connected to the lower end of the gas burette. After all the air has been expelled from the connections turn the three-way stopcock in such a position as to permit the pyrogallate to flow up into the gas burette, coming in contact with the air to be analyzed. The pressure tube should now be elevated as high as the connecting rubber will admit and the potassium pyrogallate solution allowed to run into the burette (*A*). The clamp on the connecting tube should now be applied to it close to the lower end of the burette.

Fig. 128



Position 1 Position 2 Position 3

Position of gas burettes during analysis of air. Attach a tube from the top of the gas burette (*A*) to the ventilating apparatus at *k*, Fig. 129, to catch air which has passed through the animal cage and which is escaping from *k*.

This operation made positive pressure in the burette, thereby causing a more rapid absorption of the oxygen. The burette should now be taken by the experimenter and its ends alternately raised and lowered. At frequent intervals he should loosen the clamp on the connecting rubber tube, and raise the pressure tube, thus permitting potassium pyrogallate solution to take the place of the oxygen as it is absorbed. This procedure should continue ten minutes, after which the clamp on the connecting rubber tube should be loosened. The burette and its pressure tube should be allowed to remain ten minutes longer, at the end of which time the solution in the burette should be brought to a level with the solution in the pressure tube by elevating or lowering the tube. This causes the air in the burette to be under the atmospheric pressure existing at that time. The reading for the amount of oxygen is now taken.

To calculate the amount of oxygen consumed by the animal, one subtracts the amount of oxygen found in the respired air from that found in the normal air. At least one sample should be analyzed from each ten litres of respired air, the average being used to obtain the result.

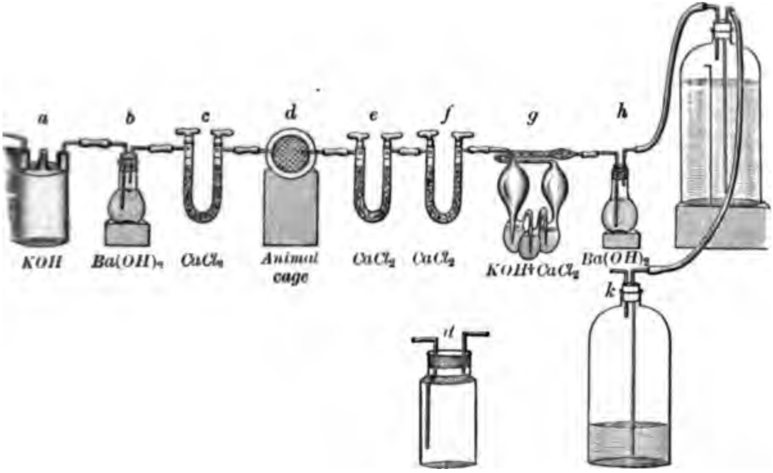
Besides the above-described direct determination of oxygen there is an indirect method given by Pembrey (Schafer's *Text-book of Physiology*, vol. i. p. 695): "The intake of O may be estimated in the following way: The animal is weighed at the beginning and at the end of the experiment, and the difference between the weights of carbon dioxide and water discharge and the loss in weight of the animal represents the oxygen absorbed. Thus, if Wi represents the initial weight of the animal, and Wf its final weight, then $Wi - Wf = w$, the loss in weight of the animal. If $CO_2 + H_2O$ represents the weights of carbon dioxide gas and water discharged during the experiment, then $CO_2 + H_2O - W = O$, the oxygen absorbed."

In most respiration experiments these two methods of determining the oxygen may be used, one method serving as a check or control observation on the other.

(*b*) **Estimation of CO_2 and H_2O Exhaled.**—A simple apparatus for accomplishing this is shown in Fig. 129. The general construction is as follows: (*d*) An animal cage, for which, for small animals like rats or guinea-pigs, a large, wide-mouthed bottle may be used; (*a*) KOH; (*b*) $Ba(OH)_2$; (*c*) $CaCl_2$, free the afferent current of air of all CO_2 and H_2O, so that the animal inspires an atmosphere of nitrogen and oxygen in proportions that may be accurately determined; (*e*) and (*f*) are calcium chloride tubes for absorption of the water, the increase in weight is equal to the water which leaves the animal cage during the experiment; (*g*) is a Geissler potash bulb for absorption of CO_2, its weight is taken before and after the observation; the $Ba(OH)_2$ flask (*h*) indicates whether all of the CO_2 has been absorbed by the potash bulbs; (*i*–*k*) is a siphon apparatus for drawing the air through the apparatus. The 10-litre bottles are graduated so that the quantity of expired air may be determined. The amount of oxygen in this expired air may be determined as above shown, and by taking the weight of the animal cage with and without the animal before and after the experiment we have data for determining: (1) the amount of oxygen consumed per kilogram animal per hour;

(II) the amount of CO_2 and of H_2O excreted per kilogram per hour. Unless the experiment is continued over considerable time the water excretion is only approximately determined. If there is no micturition or defecation by the animal the difference of weight in the calcium tubes will give the water excreted by lungs and skin. If there is micturition, a part of the water caught by the tubes will have been evaporated from the urine. If the animal be introduced into the cage just after voiding urine, and if the amount of urine in the bladder at the end of the observation be determined it will be possible to make a fairly accurate estimate of the amount of water excreted during the period of observation.

FIG. 129



Apparatus for the estimation of CO_2 and H_2O in exhaled air.

When it is desired to observe the respiration of a man or any animal too large for such an apparatus as that figured above, one has only to have a cage made large enough for the subject and supplied with a measured current of air, samples of which are measured and analyzed as it enters and as it leaves the chamber. The principle involved in the use of the large apparatus is the same as that for the small apparatus above described. The large respiratory chamber enables one to determine for a large animal or for a man the respiratory relations under various circumstances; (I) rest; (II) work; (III) fasting; (IV) various diets; (V) drugs, etc.

(*c*) **The Respiratory Quotient.**—This is the ratio between the volume of CO_2 exhaled and the volume of oxygen absorbed in the lungs. In the human subject, on an average diet, the air loses by absorption in the lungs 4.78 volumes per cent. of oxygen and receives from the blood 4.34 volumes per cent. of CO_2; hence the respiratory quotient:

$$R. Q. = \frac{CO_2}{O_2} = \frac{4.34}{4.78} = 0.908 \text{ or } 0.91.$$

The respiratory quotient varies considerably in different species, and in the same animal under different conditions. Just how these variations arise will be made clear if we study the relation of these two gases in a combustion. If one litre of oxygen at 0° C. and 760 mm. pressure unite with carbon to form CO_2, that gas at 0° C. and 760 mm. will measure exactly one litre, so that the combustion quotient of pure carbon is

$$\frac{1 \text{ vol.}}{1 \text{ vol.}} = 1.$$

Suppose now that we burn starch or cellulose, or any carbohydrate. Six molecules of oxygen (O_2) will unite with each molecule of carbohydrate to form six molecules of CO_2 and release 5 or 6 molecules of H_2O. But the H_2O is not taken into account in combustion quotients or respiratory quotients, so that the combustion quotient of a carbohydrate would be

$$\frac{6CO_2}{6O_2} = 1.$$

It must be evident that in the oxidation of carbohydrates in the animal organism the ratio would be the same—*i. e., the respiratory quotient for carbohydrates*

$$= \frac{6CO_2}{6O_2} = 1.$$

In the combustion or in the metabolism of fats the ratio is modified by the presence of a quantity of hydrogen whose oxygen is not provided for by the oxygen present in the fat molecule. Let us take tripalmitin as an example: Its formula is $C_3H_5[CH_3.(CH_2)_{14}.COOH]_3$ or $C_3H_5(C_{16}H_{31}O_2)_3$ or $C_{51}H_{98}O_6$. To oxidize the tripalmitin molecule it will require $51O_2$ to form $51CO_2$; but to oxidize the hydrogen of the molecule it will require 49 atoms of oxygen, 6 of which already exist in the molecule, leaving 43 atoms or 21.5 molecules to be supplied (51 + 21.5 = 72.5); it will require then a total of 72.5 molecules of oxygen to yield 51 of CO_2, *the combustion quotient or the respiratory quotient for tripalmitin*

$$= \frac{51CO_2}{725O_2} = 0.7034.$$

The respiratory quotient for proteids cannot be so accurately determined, but it ranges for different proteids between 0.75 and 0.81.

From what has been said it is evident that the variations of respiratory quotient must vary with the proportion of carbohydrates, fats, and proteids in the diet: (I) in herbivora it is 0.9 to 1.0; (II) in carnivora, 0.75 to 0.80; (III) in omnivora, 0.80 to 0.90.

During fasting the animal consumes its own tissues—*i. e.*, the reserve fats and proteids—and the respiratory quotient ranges from 0.70 to 0.75. In the child the respiratory quotient is lower than in the adult, due undoubtedly to the more active proteid metabolism in the growing individual. The ratio is higher in the daytime than at night, because the muscular activity is greater during the day and muscular activity is accompanied by a free katabolism of dextrose (carbohydrate) in the muscle while the muscle tissue itself (proteid) is katabolized no more during work than during rest.

The following table illustrates some of the points mentioned above:

ANIMAL.	CONDITIONS.	R. Q. = $\frac{\text{Vol. CO}_2}{\text{Vol. O}_2}$
Ox.	On carbohydrate diet. (Herbivorous.)	1.00
Horse.	On carbohydrate diet. (Herbivorous.)	1.00
Sheep.	On carbohydrate diet. (Herbivorous.)	0.88
Rabbit.	On carbohydrate diet. (Herbivorous.)	0.90–1.00
Dog.	On mixed diet. (Omnivorous.)	.9
Calf.	On milk diet.	0.86
Man.	On carbohydrate diet. (Omnivorous.)	0.8–0.90
Dog.	On flesh diet. (Carnivorous.)	0.7
Cat.	On flesh and milk diet.	0.8
Rabbit.	Fasting.	0.7
Dog.	Fasting.	0.7
Marmot.	Awake.	0.8
Marmot.	Asleep. (Hibernating.)	0.5

b. Respiratory Changes in the Blood.

1. The Gases of the Blood.—One of the functions of the blood is to carry oxygen from the lungs to the tissue, and carbon dioxide from the tissue to the lungs. The next step in our inquiry is to subject arterial and venous blood to a vacuum to determine how much oxygen and CO_2 arterial and venous blood will yield under those conditions.

(*a*) **The Method of Extracting the Gases of the Blood** is shown in Fig. 130. When subjected to a vacuum the gases leave the blood, and after being freed from moisture they may be drawn first into the fixed mercury bulb (*M*), and then, through adjustment of the three-way tap (3*T*), sent into the eudiometer (*E*), where they are collected above mercury and may be subsequently analyzed.

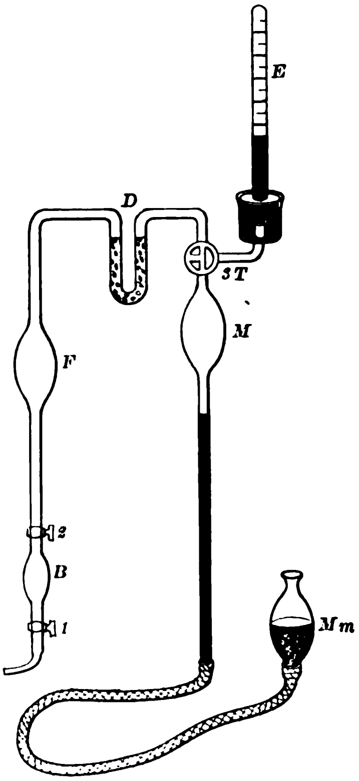
(*b*) **The Results.**—One hundred cubic centimetres of blood, whether arterial or venous, yields about 58 c.c. of mixed gases. The results may be thus tabulated:

Gas.	In arterial blood.	In venous blood from right ventricle.	Difference.
Oxygen . . .	19.6 c.c.	11.2 c.c.	8.4 c.c.
Carbon dioxide . .	36.6 "	45.3 "	8.7 "
Nitrogen . . .	1.9 "	1.9 "	
Total vol. per cent. gas	58.1 "	58.4 "	0.3 "

The observations from which the above was compiled were made upon over 160 dogs and by several different observers: Bert, Ewald, Mathieu, Schaffer, Pflüger, Setschenow, and others.

While the proportions of O and CO_2 are practically the same in different parts of the arterial system, they vary greatly in different parts of the venous system. The proportion of CO_2 is much greater in those veins which drain active tissues than in those which drain inactive ones; it would be, for example, much greater in veins from muscular tissue than in veins from subcutaneous connective tissue.

FIG. 130



Plan of apparatus for extracting the gases of the blood. To extract gases from the blood 100 c.c. of blood are drawn in the blood bulb *B* from the artery or vein. By closing tap 1 and opening tap 2, the blood is exposed to the conditions which exist in the rest of the apparatus. Suppose that the movable mercury bulb *Mm* had been previously held at the level of the fixed mercury bulb *M*; if it be lowered to the position shown in the figure there will be a rarefaction of the air in *F*, *D*, and *M*, and the gases will begin to escape from the blood. If a vacuum be previously established in the apparatus above tap 2, the turning of that tap will subject the blood to a vacuum, the gases will escape with such force as to fill the froth chamber *F* with froth or bubbles from the blood; but the drying tube *D* removes all moisture from the gases, which may be drawn through the three-way tap 3*T* into *M* by lowering *Mm*. If, now, 3*T* be turned to the left 90° and *Mm* be raised, the extracted gases will pass eudiometer *E*, where it is received above mercury and may be measured. A repetition of the process with a warming of the blood bulb will enable the experimenter to extract all of the gases.

2. **The Relations of Oxygen in the Blood.**—If the oxygen is in a state of simple solution in the blood as it is in the water—as described in the physical introduction—we shall expect it to give up its oxygen to a forming vacuum in proportion to the falling oxygen pressure. Suppose we make the experiment. (See Fig. 131.) Let the line *n O* of the figure represent the gradual fall of the oxygen pressure. If the line *x O* represents the quantity of oxygen dissolved in the blood, then, according to the physical laws given above—the Henry-Dalton

law of absorption of gases—the decrease in the quantity of dissolved oxygen would be represented also by a line $n\,O$; but the curve $n\,p\,O$ represents what actually takes place—*i. e.*, the oxygen is given off very slowly until the pressure is reduced to one-third or one-fourth, and then it escapes very rapidly and not proportionately to the pressure.

On the other hand, if the oxygen pressure is gradually increased, as in the line $O\,n'$, the quantity of that gas does not increase proportionately, but is represented by the curve $O\,p'\,n'$—*i. e.*, the oxygen is absorbed very rapidly at first and very slowly later. But we have ignored the fact that the blood is composite. Let us make the experiment with plasma, or, better, with serum. We will release only a small quantity of oxygen by reducing the pressure to zero—a quantity represented by the line $x\,P$, and the line $n\,P$ represents the gradual decrease with decreasing pressure. It appears then that the small quantity of oxygen which is associated with the plasma obeys the Henry-Dalton law, and must, therefore, be simply dissolved. If the red blood corpuscles, or, better, if a strong solution of hæmoglobin, be subjected to the same experiment, we will find that at first no oxygen is given up, then suddenly all of it is given up rapidly with the falling pressure, but not proportionately to the pressure. (See curve $H\,h\,O$.) If the pressure be gradually increased the oxygen will be taken up very rapidly at first until the hæmoglobin is satisfied, after which no more will be taken up. (See curve $O\,h'\,H'$.) The quantity of oxygen absorbed by the hæmoglobin of a given quantity of blood may be represented by the line $P\,O$. From this we find: (I) the hæmoglobin takes up vastly more oxygen than does plasma; (II) the small amount of oxygen held by the plasma is in simple solution and obeys the Henry-Dalton law; (III) the oxygen which is held by the hæmoglobin is not dissolved; it is held by chemical affinity, the combination being called *oxyhæmoglobin* and written HbO; (IV) the oxygen can be separated from hæmoglobin only at low oxygen pressure, and unites with hæmoglobin readily at much below atmospheric oxygen pressure.

FIG. 131

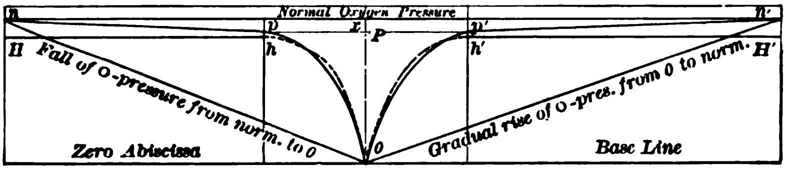


Diagram showing relation of oxygen in the blood.

3. **Relations of CO_2 in the Blood.**—We have found that less than three volumes per cent. of CO_2 represents the equilibrium of absorp-

tion of that gas in the lungs. From the physical laws above given we should expect the quantity of CO_2 in the blood to be small and the amount left in the blood after having passed the lungs—*i. e.*, the amount of CO_2 in arterial blood, to approximate the equilibrium, 3 volumes per cent.

The report of a series of experiments will aid us at this point of the discussion:

Experiments. (i) If arterial blood be subjected to a zero CO_2 pressure it will give off about 35 volumes per cent. of CO_2.

(ii) If plasma be subjected to similar conditions it will give off 13 to 26 (average 20) volumes per cent. of CO_2.

(iii) If venous blood be observed in the same way 40 to 45 volumes per cent. of CO_2 will be collected.

(iv) The red blood corpuscles alone yield under similar conditions about 15 volumes per cent. of CO_2 (5 per cent. to 7.5 per cent. of the whole blood).

(v) Plasma plus weak acid will yield *in vacuo* about 30 volumes per cent. CO_2.

(vi) Plasma plus Hb will yield *in vacuo* about 30 volumes per cent. CO_2.

These experiments and observations justify the following *conclusions:*

(i) More CO_2 is contained in the blood than can be accounted for on the basis of physical laws.

(ii) The plasma contains about two-thirds of the CO_2, and it is, for the most part, in chemical combination.

(iii) The CO_2 of the plasma must in part be held in weak chemical combination and in part in strong chemical combination, because a part of the chemically combined CO_2 is released at zero CO_2 pressure. At this point it is necessary to inquire: In what chemical combinations does CO_2 exist in the plasma? Is one of these affected by CO_2 pressure? Carbon dioxide exists in the plasma in combination with sodium as $NaHCO_3$ and Na_2CO_3. Of these two compounds the former is a weak one and at zero CO_2 pressure will part with that gas according to the following equation:

$$\begin{array}{ccc} \text{Tissues} & vs. & \text{Lungs.} \\ 2NaHCO_3 & = & Na_2CO_3 + H_2O + CO_2. \\ \text{High } CO_2 \text{ tension} & vs. & \text{Low } CO_2 \text{ tension.} \end{array}$$

Now, the addition of a weak acid, or of HbO, further decomposes the Na_2CO_3, thus liberating the last of the CO_2. The Na_2O probably joining to $2NaH_2PO_4$ to make $2Na_2HPO_4 + H_2O$.

(iv) About one-third of the CO_2 of the blood is held by the red blood corpuscles. It is supposed that this is for the most part held in a loose chemical combination with the hæmoglobin of the corpuscles; in fact, with the globulin component of the hæmoglobin.

(v) Hæmoglobin, especially oxyhæmoglobin, acts as an acid, and the more stable carbonates of the blood are broken up in the presence of HbO and *a zero* CO_2 *pressure.*

Our next task is to weave these facts and conclusions into a consistent theory. Preliminary to this let us define the word *tension* as used by the physiologist in this connection. If the partial pressure of a gas be increased or decreased the quantity absorbed will rise or fall accordingly. It is evident that the gas must be under a certain degree of pressure to prevent its passing out of solution. The gas in solution is said to be under *tension.* If the partial pressure of this gas (in the air) diminishes, the gas in solution is given off until the partial pressure of the gas in the air and the tension of the gas in solution are equal. *Tension* is expressed in the same terms as *pressure* —*i. e.*, in millimetres of mercury. The tension of CO_2 in the tissues = 7.66 per cent. of 760 mm. = 58.25 mm.; in the venous blood = 41; in arterial blood = 21.28; while the partial pressure of this gas in the alveoli equals 23 mm. of mercury. Inasmuch as the $NaHCO_3$ of the plasma will tend to change to a more stable compound, giving up one-half of the CO_2 in the lower CO_2 tension of the lungs, we shall expect to find the CO_2 passing regularly from a place of high tension to one of low tension. It will naturally then diffuse rapidly from the tissues with their tension of 58 + to the blood, which enters the capillaries of the tissues with a tension of 21 +, and leaves the capillaries *en route* for the lungs with a CO_2 tension of 41 +, nearly double what it entered the tissues with, but still considerably below tissue tension (58). It must be stated at this point that the diffusion is made possible by two things working together, both tending to take up simply dissolved CO_2 from the plasma, store it away, so to speak, in a chemical combination. (I) The hæmoglobin, which just parted with its oxygen, may now satisfy its affinities with CO_2, which it does, thus making place for more CO_2 to diffuse into the plasma. (II) CO_2 has a strong affinity for sodium. This element does not exist free or in loose combination, except with Na_2HPO_4. So that the phosphoric acid is forced to part with its second atom of sodium, as shown in the following equation:

Tissues *vs.* Lungs.

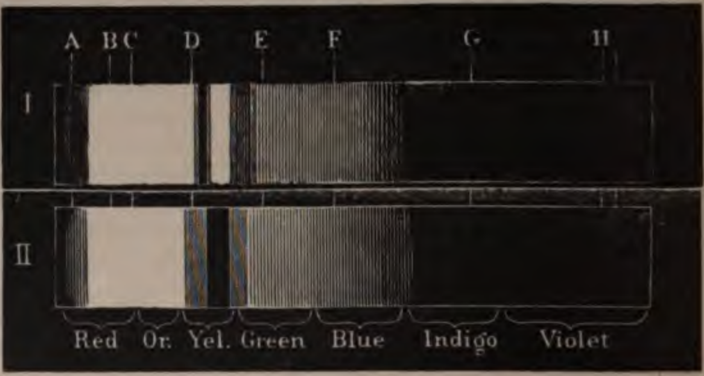
$$NaH_2PO_4 + NaHCO_3 = Na_2HPO_4 + CO_2 + H_2O.$$

High CO_2 tension *vs.* Low CO_2 tension.

The venous blood passes to the lungs, having received an increase in CO_2, which has been largely taken into such chemical combinations as $NaHCO_3$, leaving the amount dissolved in the plasma varying little probably from that which is found in the arterial blood. Reaching the lung capillaries the conditions are reversed. The high oxygen tension of the alveoli favors the reversal of the reaction between the hæmoglobin and the oxygen and carbon dioxide gas. The stronger affinity of hæmoglobin for oxygen causes it to drop the CO_2 and take up oxygen forming HbO. The CO_2 is first taken up by the plasma, thus further increasing the CO_2 tension in that liquid and further hastening diffusion toward the alveoli. Besides this interchange we must not forget that the low CO_2 tension in the lungs favors the reversal of the reaction between NaH_2PO_4 and the $NaHCO_3$.

Just how far this reaction between phosphoric acid and carbonic acid plays a part in actual respiration is still undetermined. Equally undetermined is the importance of the relation between Hb and CO_2. That the chemical reactions take place when plasma or a solution of these compounds is under experimental test is demonstrated. But we must remember that we have only to account for an addition of 6 to 8 volumes per cent. of CO_2 in the tissues and a release of the same amount in the lungs, and it is not certain that the reaction in question plays any important part in it.

Fig. 132



I, spectrum of oxyhæmoglobin ; II, spectrum of reduced hæmoglobin. (After Dalton.)

4. **The Influence of Blood Gases upon the Spectrum.**—In any spectroscopic examination of the blood account must be taken of the fact that hæmoglobin reacts very differently under different conditions: (I) When combined with oxygen as oxyhæmoglobin (HbO) it shows two absorption bands as shown in Fig. 132, I. (II) When it is deprived of its oxygen—*i. e.*, reduced to hæmoglobin—the light absorption takes place in one broad band which nearly corresponds to the two above with the space between them. (See Fig. 132, II.)

2. INTERNAL OR TISSUE RESPIRATION.

The terms *external* and *internal* respiration are used to designate different phases of the same general process. The essential process is the providing of oxygen to the active cells, where it is combined with the cell plasma either in some of the steps of anabolism or in some of the earlier katabolic steps. This ultimate step of respiration is called "*tissue respiration,*" or "*internal respiration.*" A still better term would be *cell respiration.* Cell respiration, then, consists in taking up of oxygen from the intercellular plasma and utilizing it in katabolic processes. The ultimate products of katabolism are CO_2, H_2O, etc. These end products are useless to the cell and are ejected into intercellular plasma. It is evident from this that cell respiration is simply one phase of cell nutrition which deals with the gaseous elements of assimilation (oxygen) or of excretion (CO_2). The term external respiration is applied to all those processes by which air is introduced into the lungs, the oxygen taken up by the blood, the CO_2 given off by the blood, and the transfer made with the tissue plasma. The relations between external respiration and internal or cell respiration may best be illustrated by a diagrammatic scheme of the respiration. The oxygen of the atmosphere enters the zone of tidal air where the oxygen pressure equals that of the atmosphere; from this zone it rapidly diffuses into the zone of reserve air, where the oxygen pressure is lower. Thence it diffuses into smaller bronchioles and alveoli, where the pressure is still lower (approximately 100 mm. mercury). The lower pressure of the capillaries invites it to pass through the two delicate membranes which separate it from the lumen of the capillary. Once in the blood current it is swept along as HbO to the active cells, where the oxygen pressure is practically zero. Here the hæmoglobin gives up its oxygen, or the oxygen is dissociated, is dissolved in the cell plasma in part, or passes directly into the living cells, where it is at once chemically combined in the cell metabolism.

Fig. 183

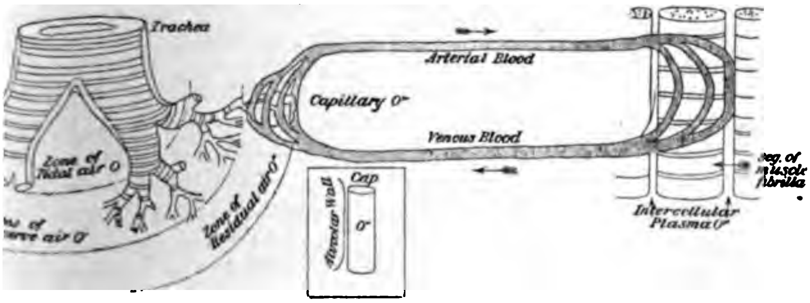


Diagram showing relation between external and internal respiration.

But the blood, now robbed of oxygen, is in the presence of very high CO_2 pressure, the hæmoglobin is instrumental in holding chemically a certain amount—let us say, provisionally, as $HbCO_2$;

the rest is taken up in simple solution in the plasma. Thus laden the blood is brought back to the air cells of the lung, where the hæmoglobin at once releases the CO_2 and takes up oxygen, forming again HbO. The CO_2 after its release from the corpuscles is in the plasma, from which it rapidly diffuses into the alveoli, because of the lo CO_2 pressure there. The relations may also be expressed thus O pressure in tidal air (158 mm.) $>$ O pressure in reserve air $>$ O pressure in residual air (100 mm.) $>$ O pressure in capillar (30 mm.) $>$ O pressure in tissues. CO_2 pressure in tidal air 0.3 mm $<$ CO_2 pressure in reserve air $<$ CO_2 pressure in residual air (23 mm. $<$ CO_2 pressure in capillary (41 mm.) $<$ CO_2 pressure in tissue (58.25 mm.).

Reichert (*American Text-book of Physiology,* p. 526) uses th following very effective method to show why the O passes from the alveoli of the lungs into the blood and CO_2 in the reverse direction:

	O	CO_2
Tension in alveolar air	100	23
Pulmonary membrane	↓	↑
Tension in venous blood	22 +	41 +
Absorbed by venous blood	7.2 vol. %;	lost 8.2 vol. %.

In a similar way he shows graphically why the diffusion currents are reversed in the tissues:

	O	CO_2
Tensions in arterial blood	29.64	21.28
Bloodvessel walls	↓	↑
Tensions in tissues	0.0	58.25
Lost in tissues	7.2 vol. %;	gained 8.2 vol. %.

Having defined the external and the internal respiration and having shown the forces which operate in the movements of the gases of respiration, it remains to treat briefly the relation of cell respiration to general cell metabolism. This has been done in some detail under General Physiology, so that a brief summary is all that is here required.

Summary of the Principles of Cell Respiration.

(I) The increase of the supply of oxygen does not increase the activity of the cell or tissue.

(II) The increase of cell activity is accompanied by an increase of need for oxygen followed by an increase of the supply of oxygen.

(III) The amount of CO_2 given off by the cell is proportional to its activity; and is, therefore, *a measure of cell activity.*

(IV) Cell activity takes the form of *liberation of energy.* This energy is the potential energy of cell protoplasm (or energy producing material held by the protoplasm—see Metabolism) and is liberated not by direct oxidation, as in combustion, but by indirect oxidation.

By integration of O a force-yielding storage substance is formed." aller.)

ỳ disintegration of this substance carbon dioxide is liberated in ıpany with other material katabolites and energy in the form of t, work, and electricity.

C. THE CONTROL OF THE RESPIRATION.

1. INNERVATION OF THE RESPIRATORY ORGANS.

a. General Experiments and Conclusions.

ι dissection of the respiratory system would reveal the presence :he intercostal nerves, one just posterior to each rib, giving off branches to the intercostal muscles; followed toward the central vous system, these nerve trunks are found to emerge from the ıal cord by two roots, an anterior nerve root and a posterior ve root. One would find the diaphragm supplied by a pair of e nerves, which may be traced up through the mediastinum of the thorax into the deep muscles of the neck, where they found to be a part of the cervical plexus and to arise from the IV and V cervical nerve roots; these are the phrenic nerves. ther, we remember that the vagus gave off, besides the cardiac nches, the superior laryngeal and inferior laryngeal, and the aining trunk is largely distributed to the tissue of the lungs, ıgh a part of the trunk extends into the abdomen. If we follow distribution of the vagus in the lungs we will find that its branches r the root of each lobe, and are distributed along the air passages plying the mucous membrane and the involuntary muscles of bronchioles. Physiologic experiment alone can determine the on of these different nerves.

. **Experiments.**—(I) Cut one or more of those lower intercostal es which supply the abdominal muscles; the muscles will cease ıct in expiration.

I) Cut one or more of those upper intercostal nerves which supply external and internal intercostal muscles; the muscles in question e to act—*i. e.*, the external intercostals cease to elevate the ribs nspiration and the internal intercostals cease to depress the ribs xpiration.

II) Cut the posterior nerve roots of any of the intercostal nerves; results above observed in cutting the whole nerve trunk are not d in this case.

V) Cut the anterior nerve roots of any of the nerves in question; result is the same as if the whole trunk were severed.

) Cut the phrenic nerve; the diaphragm ceases its active movets, though it will continue to move passively so long as the respiratory movements are kept up through the agency of the intercostals.

(VI) Cut the vagi; inspiration is deeper and the respiratory movements slower.

(VII) Cut the superior laryngeal; a tickling of the larynx will no cause coughing expiration.

(VIII) Cut the inferior or recurrent laryngeal; all contractions of glottis and tracheal muscles cease.

(IX) Cut the spinal cord just above the first intercostal; all respiratory movements of the ribs and of the abdominal muscles cease.

(X) Cut the spinal cord just posterior to the medulla oblongata; all respiratory movements of the ribs, diaphragm, and abdominal muscles cease, but the glottis, larynx, and nostrils will make spasmodic inspiratory movements.

(XI) Cut or sever brain from medulla, everything else being intact; the rhythm and the depth of the respiratory movements are not disturbed. Excite the animal; no change or depth of rhythm.

(XII) Separate the two lateral halves of the medulla by sagittal incision in the median line. The respiration continues as before, but destruction of one side of the medulla causes respiratory movements to cease on that side.

2. **Conclusions from These Experiments in Order.**—(I) Th lower intercostal nerves carry motor fibres of expiration.

(II) The upper intercostal nerves carry motor fibres of both inspiration and expiration.

(III, IV) The moter fibres out of the spinal cord *via* the anterio nerve roots.

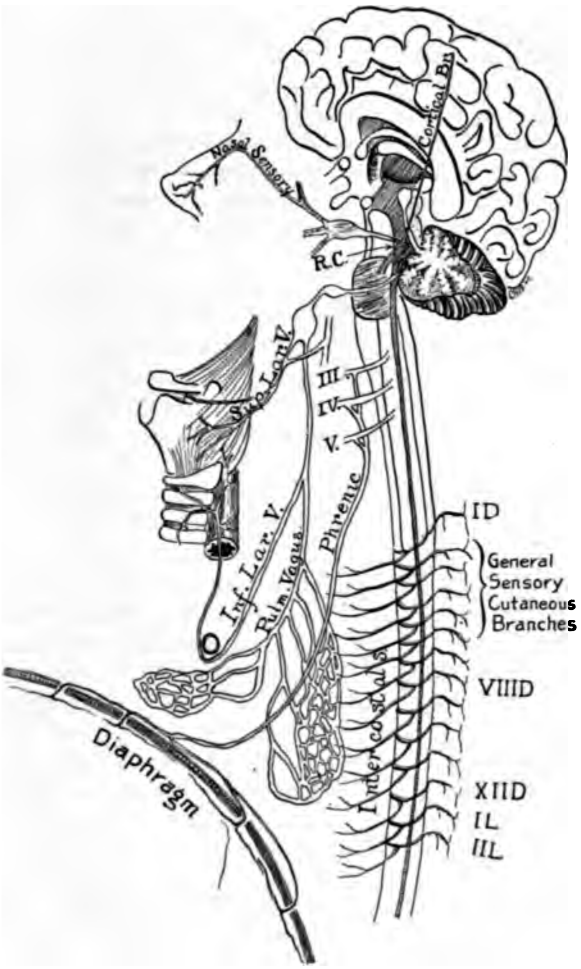
(V) The phrenic nerve is the motor nerve of the diaphragm, and therefore, a motor nerve of inspiration. Each phrenic innervate the corresponding side of the diaphragm.

Any of these conclusions may be verified by stimulating the dista end of any of the cut nerves; in every case the muscles supplied wil contract, showing the nerves to be, in part at least, efferent moto nerves.

(VI) From experiment (VI) it is difficult to say exactly what th function of the vagus is. Inasmuch as the nerve is supplied largel to mucous membranes, we cannot expect it to be motor in its action Suppose the distal end be stimulated; no very noticeable change take place. Now stimulate the central end; respiratory movements ar at once affected. A carefully adjusted stimulus of the central ends ma lead to normal respiratory movements. A strong stimulation to th central end of the vagus will lead to a more rapid fate of respirator movements and a final standstill of the diaphragm either at the en of expiration or inspiration—*i. e.*, diaphragm either in tetanus or i paralysis. These results prove the vagus to carry ***afferent*** or ***sensor*** fibres, and the ambiguous results may be accounted for as the resul *of two kinds of sensory fibres,* one kind stimulating the inspiratory centre and another kind stimulating the expiratory centre.

(VII) The superior laryngeal is a sensory nerve stimulating explosive expiratory acts.

FIG. 134



Schema of innervation of respiratory organs. *R.C.*, respiratory centre in the medulla; *V.*, vagus with superior laryngeal, inferior laryngeal, and pulmonary branches. Phrenic supplying the diaphragm; intercostals supplying the inspiratory and expiratory muscles of the thorax and the expiratory muscles of the abdomen. All cutaneous sensory nerves affect the respiratory centre. Nasal sensory may precipitate sneezing or otherwise affect respiration.

(VIII) The recurrent laryngeal is the motor nerve of the glottis and of laryngeal and tracheal muscles. Stimulation of the distal end confirms the conclusions, for the muscles of this region contract vigorously.

(IX) The respiratory centre for intercostals and abdominal muscles is above the dorsal cord.

(X) The general respiratory centre is not posterior to the medulla.

(XI, XII) The general respiratory centre is not anterior to the medulla. The *centre is located in the medulla*, in the floor of the fourth ventricle, just posterior to the cardioinhibitory centre. It is found to be symmetrically located in the two lateral halves; though these communicate and act in harmony they may be separated and still act synchronously, but may be made to act inharmoniously by special stimulation of one-half. Each half is further believed to consist of an inspiratory and of an expiratory nucleus. From experiments (X) and (XI) it is clear that the *centre is automatic*. From experiments (VI) and (VII) it is shown that the *centre is also reflex*.

b. The Action of the Respiratory Centre.

1. **Through its Automatic Action** the centre would send intermittent *spasmodic inspiratory* or *expiratory* impulses along the efferent nerves to the respiratory muscles. The automatic action of the respiratory system is analogous to that of the circulatory system.

2. **Direct Stimulation** may be accomplished through the influence of blood supply. (α) *The Influence of CO_2 and O in the Blood Supply.* In this connection we remember that the cardiac centre in the medulla is affected by the quantity and quality of the blood which it received from the heart through the carotid and vertebral arteries. In a similar way the respiratory centre is affected by blood from the same source. In this case the quality of blood is of more importance than the quantity—*i. e.*, it is the quantity of oxygen and carbon dioxide which stimulates the centre. The inspiratory acts as modified by the stimulating presence of an excess of CO_2 in the respiratory centre, while the respiratory are less affected by the CO of the blood until this accumulates to an abnormal degree; even then it may be rather lack of oxygen than excess of CO_2 which causes the change in the respiratory movements. Frederick performed a most interesting experiment with two dogs. The vertebral arteries were ligated; the carotids of dog A were joined through cannulæ to the distal end of those of dog B, and those of dog B connected with those of dog A, so that blood of dog A circulated in the head of dog B and *vice versa*. The experiment consisted in suddenly closing the trachea of dog A; after a few moments dog B began to gasp for breath. The reason is clear; the excess of CO_2 from the circulation of dog A stimulated the respiratory centre of dog B, leading to his much increased respiratory movements.

(β) *The Influence of the Temperature of the Blood Supply.* If the carotid arteries of a dog be enveloped in ice the respirations decrease in rate; if enveloped in cotton saturated with water several degrees above blood temperature, the rate will be noticeably increased.

The common observation of increased rate in fevers is another illustration of the same thing.

3. **Reflex Stimulation** of the centre is an important factor in the control and rhythm and depth of the respiratory movements.

(α) *The Direct Vagus Influence* is of first importance. When the lungs become distended to a certain degree the sensory fibres of the vagus send an impulse to the centre which precipitates an expiration. Again, an impulse from the superior laryngeal may cause a spasmodic contraction of the abdominal muscles causing a cough. Certain irritating gases, Cl, SO_2, etc., affect these sensory nerves of the nose and larynx, and cause the centre to block all respiration. Such gases are called irrespirable.

(β) *Indirect Reflex Stimulation* of the respiratory mechanism may be correctly so distinguished because the respiratory act is induced or influenced by impulses from nerves only indirectly connected with the respiratory mechanism. A sudden dash of cold water will cause an inspiration. When a child is being delivered feet first at birth care must be taken that the delivery be made rapidly, or that the body be protected from draughts of air, for the stimulation by the air may cause inspiration and the child may draw the respiratory passages full of mucus, which will greatly complicate the induction of normal respiration.

4. **Cerebral or Voluntary Influence on the Respiration.**—Besides the automatic action and the reflex influence of the centre, there is a marked influence from the cerebrum. In fact, if one gives his attention to it he may govern his respiratory movements as to rhythm and depth up to a certain point. Certain states of mind may modify respiration—coughing, crying, sighing, etc. One cannot, however, voluntarily stop respiration long enough to take his life. The accumulated impulses finally become too strong to be controlled by the mind and the diaphragm descends.

2. UNUSUAL RESPIRATORY CONDITIONS.

In contradistinction to the usual and normal respiration, which is called EUPNŒA, there are several conditions which deserve mention.

1. **Apnœa.**—Complete cessation of respiration. One can "hold his breath" much longer if he precedes his efforts by a series of rapid, deep breaths. If the air be vigorously and rapidly forced into the lungs of an animal by artificial respiration for a minute, some time will elapse before the animal evinces any tendency to breathe. The most natural inference—that he has oxygen enough to last a minute or two—is not the correct inference, for experiment

has shown that the blood may accumulate a marked excess of CO_2 before the centre is able to overcome inhibition, which it is receiving from some source. And what source? From the overstimulated sensory ends of the vagus.

2. **Hyperpnœa.**—Usually deep breathing, such as one is led to from too strenuous muscular exertion.

3. **Dyspnœa.**—Painful breathing. All conditions which diminish the O or increase the CO_2 in the blood circulating through the medulla, if carried beyond a certain point, produce a labored respiration, which can no longer be recognized as hyperpnœa. All the phenomena of extreme forced respiration, together with signs of the greatest discomfort, or even pain, make up the symptom-complex of dyspnœa. It is not an infrequent symptom of disease, and may occur under the following conditions:

(*a*) **Direct Limitation** of the *activity* of the *respiratory organs:* (I) *Diminution* of *respiratory* surface, as in pneumonia, or acute œdema of lungs. (II) *Entrance* of air or fluid into *pleural cavities* —pneumothorax and hydrothorax. (III) Obstruction of trachea or larynx: croup, strangulation, etc. (IV) Contraction of bronchioles—asthma.

(*b*) **Enfeeblement of Circulation.** (I) In degeneration of heart muscle. (II) Valvular disease of heart.

4. **Asphyxia.**—This term is used to express the condition of collapse after a failure of the system to get O or to eliminate CO_2. Such a condition is always preceded by (I) *Hyperpnœa,* (II) *Dyspnœa,* and (III) *Convulsions.* Death by asphyxia occurs in four stages, the three just noted, followed by *collapse* and *death.* The term is used to indicate death by drowning, by suffocation, by strangulation, etc.

D. THE LARYNX.

1. SUMMARY OF THE ANATOMY OF THE LARYNX.

From the standpoint of the physiologist, the following anatomic facts are important:

a. The Skeleton of the Larynx.

The skeletal foundation of the larynx consists of nine cartilages, of which five are physiologically important.

1. **Thyroid Cartilage.**—This is the largest, and it gives to the larynx its characteristic shape. The prominent anterior aspect of this cartilage may be felt in the throat. The flattened sides make it evident that a cross-section of the larynx would reveal for the thyroid a triangular outline, with apex forward. The posterior segment is absent.

2. **The Cricoid Cartilage.**—This is a complete ring fitted inside and below the thyroid, to whose inferior cornea it is articulated laterally. The anterior aspect of the cricoid is narrow, while the posterior aspect is wide, coming well up into the thyroid space.

3. **The Arytenoid Cartilages.**—These cartilages are attached to the upper posterior margin of the cricoid cartilage. The general outline of one of these cartilages is approximately triangular, and the articulation is such as to allow the cartilages to rotate around an axis parallel to the axis of the larynx, moving in a plane at right angles to the axis of the larynx. When the arytenoids are in a position of rest, one side coincides approximately with the anteroposterior line of the larynx. The anterior angle serves for the attachment of the vocal cords and is called the *processus vocalis.*

The axis of rotation of the two arytenoid cartilages is displaceable.

4. **The Epiglottis.**—This is a thin, spatulate cartilage, above the anterior superior margin of the thyroid; its principal function seems to be the protection of the larynx during deglutition.

b. The Muscles of the Larynx.

There are five muscles or pairs of muscles which are important to the physiologist:

1. **The Transverse Arytenoid Muscle.**—This passes from one arytenoid cartilage to the other. Its contraction tends to draw these bodies toward the median line.

2. **The Posterior Cricoarytenoids.**—Each of these two muscles has its origin on the cricoid cartilage. After passing upward and outward each is inserted into an arytenoid cartilage. Contraction of these muscles tends to rotate the arytenoid cartilages upon their axis, so that *the processus vocalis is abducted.* (See Fig. 135, *P.C.A.*)

3. **The Lateral Cricoarytenoids.**—The origin is on the inner lateral aspect of the cricoid cartilage. Passing upward and backward, each is inserted into the outer aspect of the corresponding arytenoid. Contraction of these muscles tends *to adduct the processus vocalis.* (See Fig. 135, *L.C.A.*)

4. **The Thyroarytenoid Muscles** arise from the inner anterior aspect of the thyroid, and pass directly back in the plane of the vocal cords to be inserted into the outer anterior side of the arytenoids. Contraction of the thyroarytenoids alone would adduct. This pair of muscles is involved especially in the *"fixing" of the arytenoid cartilages.*

5. **The Cricothyroid Muscles** arise on the lower posterior part of the thyroid cartilage, externally, and pass downward and forward to be inserted into the cricoid cartilage. Contraction of these muscles lifts the anterior segment of the cricoid cartilage, or at least draws the anterior segments of the thyroid and cricoid cartilages nearer

together. The result of this is to carry the upper posterior margin of the cricoid cartilage farther away from the upper anterior part of the thyroid cartilage. In other words, *to increase the distance between the two points of attachment of the vocal cords.* The cricothyroids are *tensors of the cords.*

c. The Innervation of the Larynx.

(*a*) **The Sensory Nerve** of the larynx is the *superior laryngeal* branch of the vagus.

(*b*) **The Motor Innervation** is through the *inferior laryngeal* fo all the muscles except the Cricothyroid—*i. e.*, the tensors of th cords. These muscles are innervated by the superior laryngea From this it is clear that with loss of sensation of the larynx there loss of proper phonation.

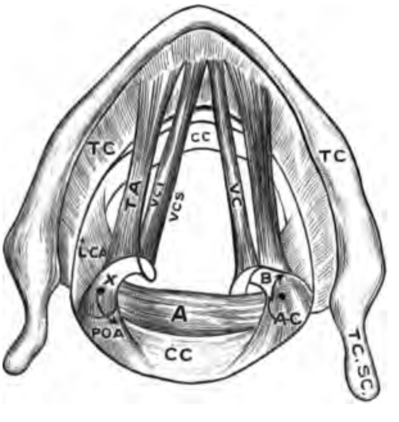
2. THE MECHANICS OF THE LARYNX.

In the diagrammatic representation of the larynx as seen from above—*i. e.*, in line of its axis—note especially the following features:

T.C. = Thyroid cartilage.

S.C.T.C. = Superior cornu of the thyroid cartilage.

Fig. 135



Diagrammatic representation of the larynx as seen from above

C.C. = Cricoid cartilage, posterior superior aspect.

A.C. = Arytenoid cartilage.

x. = Axis of articulation of an arytenoid cartilage.

T.A. = Thyroarytenoideus muscle.

A. = Arytenoideus muscle.

P.C.A. = Post. Cricoarytenoideus. (See also Fig. 136.)

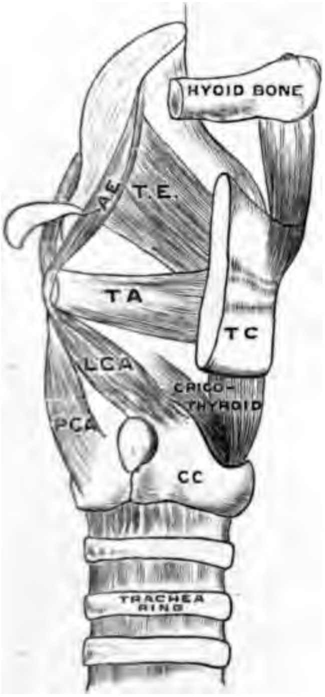
L.C.A. = Lateral Cricoarytenoideus muscle. (See also Fig. 136.)

V.C., *the vocal cords*, are attached anteriorly to the inner surface of the upper anterior segment of the thyroid cartilage and posteriorly to the processus vocalis of the two arytenoid cartilages, respectively. From the figure given it would seem that the Arytenoideus and Posterior Cricoarytenoidei would act together in rotating the arytenoid cartilage about the axis *x* in the direction of the arrow *a*. Also that the thyroarytenoidei and the lateral cricoarytenoidei would act together in the reversed rotation as indicated by the arrow *b;* furthermore, that the first action would tend to separate the vocal cords, while the second would approximate them.

But this is only a part of the truth. The axes of rotation of the arytenoid cartilages are not fixed; *they are displaceable.*

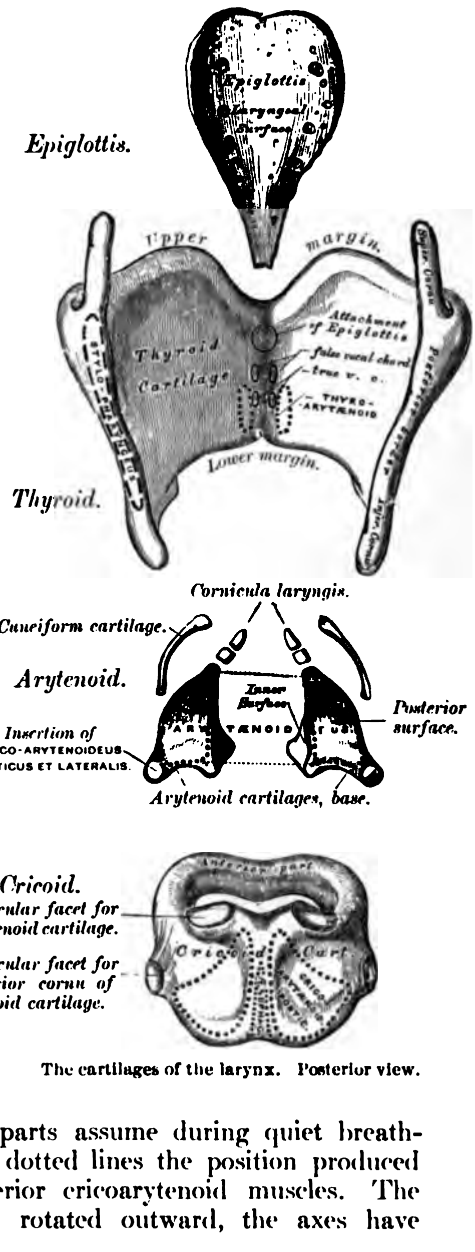
1. The Abduction of the Glottis.—In the three diagrammatic figures (Fig. 138, *A)* the continuous lines represent the larynx *at rest*—*i.e.*, in the position which the parts assume during quiet breathing. Fig. 138, *A*, shows in the dotted lines the position produced by a contraction of the posterior cricoarytenoid muscles. The arytenoid cartilages have been rotated outward, the axes have

Fig. 136



Lateral view of laryngeal muscles.

Fig. 137



The cartilages of the larynx. Posterior view.

been displaced outward, and the opening has changed from triangular to pentagonal. This position is assumed in deep inspiration. These muscles are sometimes called *abductors of the glottis,* because they separate the lateral boundaries of the glottis from the median line.

2. **The Adduction of the Glottis.**—Adduction of the lateral boundaries of the glottis may be accomplished in two ways:

(*α*) ADDUCTION BY ROTATION of the arytenoid cartilages on their axes and approximation of vocal cords alone. This is done by the *Thyroarytenoidei* muscles acting alone or in conjunction with the lateral Cricoarytenoidei. (Ses Fig. 138 *C*.)

(*β*) ADDUCTION BY DISPLACEMENT of the arytenoid cartilages toward the median line, by the contraction of the *Arytenoideus* muscle, supplemented by the *Thyroarytenoidei* and the *lateral Cricoarytenoidei.* The action of the last muscles being clearly to overcome the tendency of the Arytenoideus to rotate the tips of the cartilages outward. This second form of adduction completely closes the larynx, and the groups of muscles which perform the act are often called the *Sphincters of the Larynx.* (See Fig. 138, *B*.)

FIG. 138

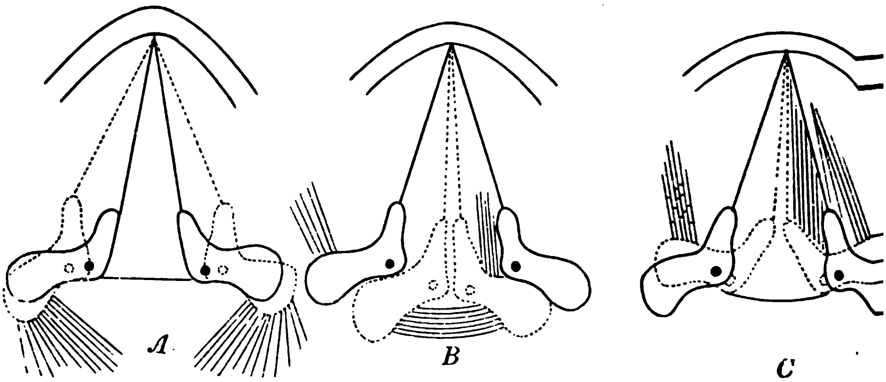


Diagram showing the action of the laryngeal muscles.

3. **The Tension of the Vocal Cords** necessary to the production of sound is brought about by the combined action of the adductors (*b*), which simply approximate the cords, and the Cricothyroidei, whose contraction brings the ventral edges of the cricoid and thyroid cartilages nearer together, separates their dorsal aspects, and thus puts the vocal cords on the stretch.

4. **The Levers of the Larynx** are levers of the first class.

3. THE ACOUSTICS OF THE LARYNX.

The larynx is a musical instrument supplied with a device for setting the air into vibration. The air thus set to vibrating is not imply the air that is being emitted from the respiratory organs, ut the air which fills the air passages of the lungs. Even the tissues f the chest and head participate, to a limited extent, either as esonating or as reflecting surfaces. The rate of vibration is deteriined wholly by the vocal cords acting as vibrating strings. The itch of voice depends, then, solely upon the vocal cords, while the mbre or quality depends upon the size of the chest and the size and pace relations of those parts of the respiratory passages, including he mouth, external to the vocal cords.

How does the pitch of the voice vary? We have only to apply he laws of the transverse vibrations of strings to the solution of the roblem. If we let l equal the length of the string, r its radius, its density, t the tension with which it is stretched, and N the iumber of vibrations per second, we would have the following ormula (for derivation see *Physiological Acoustics*):

$$(1) \qquad N = \frac{1}{2rl} \times \sqrt{\frac{t}{\pi d}}.$$

Now π and 2 may be discarded when we express it as a variable, o we would have:

$$(2) \qquad N \text{ varies as } \frac{1}{rl}\sqrt{\frac{t}{d}}$$

We see, then, that the number of vibrations per second—*i. e.*, the itch of the voice—depends upon four variables, and we may express hem separately thus:

$$\text{(I) } N \text{ varies as } \frac{1}{r}; \qquad \text{(II) } N \text{ varies as } \frac{1}{l};$$

$$\text{(III) } N \text{ varies as } \sqrt{t}; \qquad \text{(IV) } N \text{ varies as } \sqrt{\frac{1}{d}}.$$

These laws apply to the human voice in the following manner:

(*a*) *The pitch varies inversely as the radius of the vocal cord,*

$$\left(N \text{ varies as } \frac{1}{r}\right),$$

but the radius of the vocal cord varies with (I) *age*, becoming thicker with advancing age; (II) with *sex*, being thinner in females than in males; (III) besides these general variations of pitch which depend upon age and sex there are *individual differences* which lead to difference of pitch in two persons of the same age and sex.

(*β*) *The pitch varies inversely as the length,*

$$\left(N \text{ varies as } \frac{1}{l}\right).$$

The length of the vocal cords vary with (I) *age*, for they take a part in the general body growth. They vary also (II) with *sex*, reaching in the average man a length of 15 mm., while in women they are but 11 mm. in average length.

(γ) *The pitch varies as the square root of the tension* (N varies as $\sqrt{t}$). The tension varies solely with the muscular activity of the muscles of phonation. (See above.)

It may be interesting to note here that in raising the pitch of the voice voluntarily from any chosen key-note to its fifth—*i. e.*, from *do* to *sol*—whose number of vibrations would represent the ratio $\frac{3}{2}$ when compared with the key-note, it would require a tension of $\frac{9}{4}$ the original tension, or $2\frac{1}{4}$ times the original tension to produce $1\frac{1}{2}$ times the original number of vibrations per second. From this it is evident that the production of high notes must be a severe physical tax upon the muscles of phonation.

(δ) *Pitch varies inversely as the square root of the density,*

$$\left(N \text{ varies as} \sqrt{\frac{1}{d}}\right).$$

But in the human vocal cords there is no essential variation in the density of the vocal cords with age, sex, or other variable factors; so that this law does not apply to the larynx, though it does to other musical instruments.

4. THE VOICE: PHONATION.

Man possesses the function of phonation in its highest form. All animals which possess a voice are able to use it in expressing, to their associates, the various emotions and passions which move the animal mind. In most of the higher mammals phonation takes on two forms: (I) Articulate phonation, in which the voice comes in short vowel tones with consonants marking the beginning of the tone (the dog's "bow-wow," the cat's "meaw," the cow's "mōō"). These are all *words;* they are used to express the passions, the emotions, or the desires of the animals. Man possesses a series of these monosyllabic race words which take the form of exclamatory grunts, cries, shrieks, cooings, guffaws, etc., through which every passion of the human soul is instantly made known to every member of the genus *Homo* within range of the voice. Most races have developed articulate phonation into a complicated succession of articulated sounds called *speech,* through the agency of which various shades of meaning may be communicated to one's associates, and a sustained and continuous succession of ideas be communicated to the hearers. (II) Unarticulated continuous phonation or song, used primarily in the expression of the more pleasurable emotions, also of pathos.

a. Speech.

The highest form of articulate phonation is called speech. The simplest existence of a member of civilized society requires of an individual a vocabulary of 300 to 500 words in the expression of his thoughts—emotions, desires, etc. Some individuals use in the course of a year many thousand different words in the expression of their thoughts. The full vocabulary is no greater tax upon the vocal apparatus than is the scanty one, because no one language possesses more than 30 to 50 different elementary sounds; and words represent various combinations of these elementary sounds. Elementary sounds are made: (I) either with open organs of articulation, and modified in *quality* by various positions of the resonating surfaces, *vowels;* (II) or with the articulating organs: lips, tongue, teeth, and palate obstructing, more or less, the passage of the sound or breath, *consonants.* In one sense speech consists of a series of vowel sounds separated from each other (articulated) or *joined to each other* by a series of consonants.

The Vowels of the English language are a, e, i, o, u. König gives the fundamental vowel positions of the modifying organs as resulting in the five vowel sounds: ōō, ō, ä, ā, ē. All other English vowel sounds are formed of combinations or modifications of these fundamental tones. The English ī (long i) is a combination of ä, ē; the English ū (long u) is a combination of ē, ōō. Important modifications are made by changes in the quantity of the vowel sound. The English language has at least seventeen recognized vowel sounds.

The Consonants of the language may be classified on the basis of their acoustic qualities as *liquids* or semivowels: m, n, l, r, s, w, y[1]; and mutes, including all the remaining consonants. On the basis of the mechanism of formation consonants may be classified as: (I) *explosives,* as b, p, d, t, k, g; (II) *aspirates,* as f, v, w, s, th(in), l, sh, ch, h; (III) *vibratives,* as r; (IV) *resonants,* as m, n, ng. Brücke gives the fundamental consonant positions as follows: (I) articulated between the lips, *labials;* (II) articulated between tongue and hard palate, *palatolingual;* (III) articulated between tongue and back portion of hard palate or the soft palate; (IV) articulated between the two vocal cords. (Figs. 139 to 152 illustrate the articulation of consonants.)

The following table of consonants embodies the ideas of Brücke in a form somewhat better adopted to the English consonant sounds:

PLACE OF ARTICULATION.	ORAL.				NASAL.
	Momentary.		Continuous.		Continuous.
	Aspirates.	Vocals.	Aspirates.	Vocals.	Vocals.
Labials	p	b	......	w	m
Labiodentals	......	......	f	v	......
Linguodentals	......	......	th(in)	th(e)	......
Palatolinguals:					
Anterior position	t	d	s	z, l	n
Middle position	ch	j	sh	zh, r	......
Posterior position	k	g	......	y	ng

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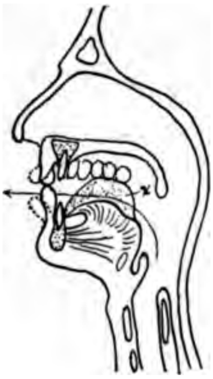
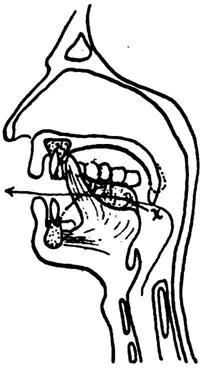
[1] *y* sometims replaces *i* as a pure vowel.

FIG. 139



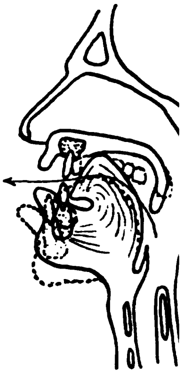
P and B

FIG. 140



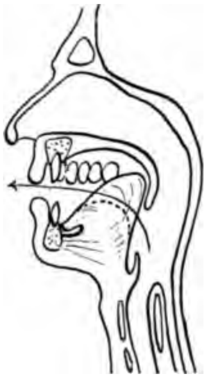
T and D

FIG. 141



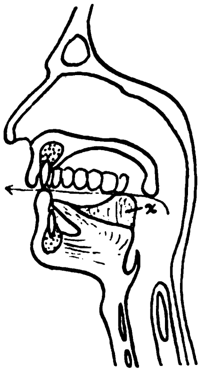
Ch and

FIG. 142



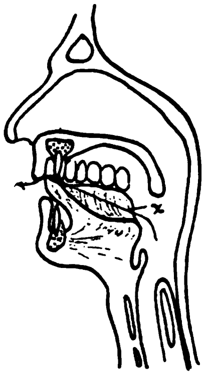
K and G

FIG. 143



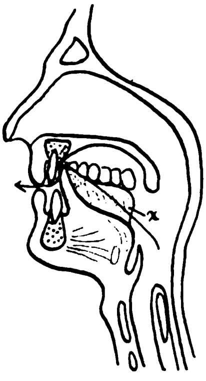
F and V

FIG. 144



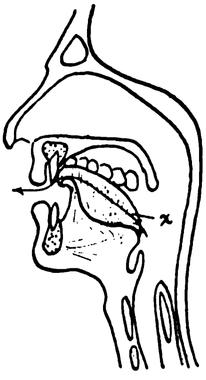
Th (in) and (

FIG. 145



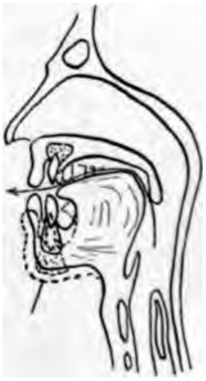
S and Z

FIG. 146



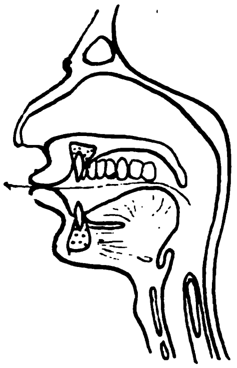
L

FIG. 147



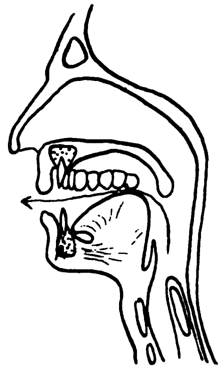
Sh, Zh, R

FIG. 148



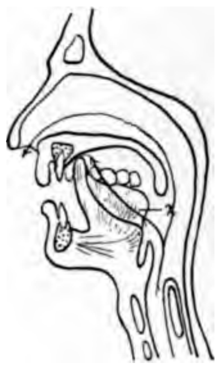
W

FIG. 149



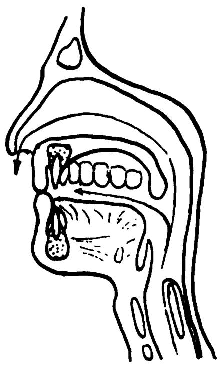
Y

FIG. 150



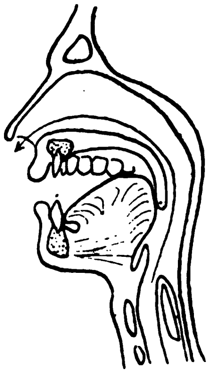
N

FIG. 151



M

FIG. 152



Ng

The relation of speech to the central nervous system is discussed at length under the *Physiology of the Brain* (*q. v.*).

b. Song.

The musical scale is discussed under *Physiological Acoustics* (*q. v.*). Though the human ear is able to appreciate a range of musical tones from a vibration rate of 16 per second up to 16,700 or 33,408 per second—*i. e.*, a range of ten or eleven octaves—the human voice is able to cover a range or compass of *two octaves* only, in rather rare cases of three octaves. The two-octave range of the male voice is below that of the female voice. The reason for this is discussed above.

PATHOLOGIC PHYSIOLOGY OF RESPIRATION.

INTRODUCTION.

From the foregoing pages it will be properly inferred that the rate, rhythm, and character of respiratory movements depend very largely upon the extent to which the blood is oxygenated as it passes through the lungs; further, that any marked inefficiency in the mechanics of respiration will of necessity decrease the amount of oxygen available in the lungs, and through stimulation of the respiratory centre in the medulla excite to increased activity such accessory mechanisms as may be necessary to raise the intake of oxygen to the required standard. Could it be assumed that there was but a mere reciprocal relation between oxygenation and a respiratory rate, a few formulæ would enable one in any case to determine with mathematical accuracy to what extent and how the lungs were involved, and whether the involvement was or was not dangerous to life. But there are many other factors which enter into this really complex problem and render its solution a difficult matter.

Take, for instance, the rate of respiration in lobar pneumonia, and the following questions might be asked: In what manner and to what extent does the attendant pleurisy influence the rate and character of respiratory movements? How do temperature, toxæmia, and bacteræmia influence the medullary centres? What is the comparative rate of diffusion through a healthy mucous membrane and one thickened by inflammation and covered by exudate? These and many other questions which might be asked along this line serve to show that any problem in this field may, to different minds, be susceptible of different solutions; that while theories are necessary in this as in other fields of investigation, they must be understood to be of utility only as working hypotheses, to be abandoned if untenable; that positive statements cannot be made except where they can be upheld by a wealth of conclusive experimental and clinical data.

The scope of this work precludes a consideration of each respiratory disease as a clinical entity, since in many of them we find almost identical pathologic conditions, combined differently or occurring in different sequence. Hence, those diseases which will be considered as to pathology and symptoms will be selected, not because of their absolute importance as diseases, but on account of the pathologic conditions from which they arise and to which they give expression. Further, not only will the local pathology and symptoms be considered, but any systemic disturbance arising from the local lesion will be discussed.

h the foregoing plan of study clearly in mind, it will be well to d directly to the consideration of the principal morbid processes ch the respiratory tract is subject, together with the attendant oms of physiologic expressions of disease, the aim being to ate each symptom with its causative pathologic process or ses.

onsidering acute inflammations of the respiratory tract, it will ted that the pathology is very similar throughout, the only nces being due to variations in the histology. At the same he variations in symptoms will be shown to be very largely the particular area of mucosa involved. In the same manner *c lesions* are due to certain definite changes in structure, and may occur at any point along the respiratory tract and be ned in very complex fashion. The mucosa may show any of lowing changes: It may be thickened, a result of proliferation, is thickening may be general and uniform, or it may be local- n which case polypi or similar growths occur, as a result of re or impaired nutrition it may become thinned or atrophic, its nutrition is completely cut off necrosis and ulceration

submucosa likewise may show uniform hypertrophic or lastic changes, or, if the changes are not general, granular or ry outgrowths occur. After a certain degree of hyperplasia eveloped, the nutrition becomes impaired by contraction of w-formed fibrous tissue and atrophy necrosis and ulceration

night be inferred from the complicated pathology, the symptoms onic respiratory diseases are not clear-cut, but vary with the s in pathology, the extent to which the tract is involved, e causative or accompanying disease. For this reason it will possible to discuss the symptomatology even briefly, and only general statements will be made. The same general rules as which apply in acute inflammatory states may be considered d true in chronic cases. The evidences of acute infection, of , are wanting, but in other respects the symptomatology of c diseases resemble those of corresponding acute conditions, more extended in their course, and often accompanied by c incurable systemic diseases—as cardiac or renal.

le from this, irritation, whether from secretion or irritating new- l tissue, produces cough and pain or discomfort; œdema or her obstructive lesion results in dyspnœas of varying degree; and long-continued coughing paroxysms will cause dilatation bronchi and alveoli, with a variety of subsequent changes. r, these chronic diseases may be but local expressions of ic disorders, as syphilis, tuberculosis, and diabetes.

functions of the upper respiratory passages are: (1) to transmit air to and from the lungs; (II) to warm; (III) to filter the inspired air; (IV) to furnish a *locus operandi* for the peripheral apparatus of the sense of smell. Therefore, any disease affecting this part of the respiratory tract will be attended by some perversion of these functions in addition to the systemic effects of an infection which may reasonably be considered in most cases to be a prime factor in the production of the morbid process. This brings up for consideration a very common disease of the upper respiratory tract—coryza, or nasal catarrh.

1. CORYZA.

a. Acute.

1. **Pathology.**—Coryza is a disease due probably to bacterial activity and is characterized pathologically by (I) catarrhal inflammation, (II) œdema, and (III) venous engorgement of the nasal and adjoining mucosa and submucosa: following this occurs degeneration and desquamation of the cells of the mucous membrane.

2. **Symptomatology.**—Symptoms in a typical case are (I) headache; (II) chilliness; (III) malaise; (IV) pains in back and limbs; (V) fever; (VI) stuffy feeling in the head; (VII) partial or complete loss of the sense of smell and perception of flavors, and sneezing.

3. **Physiology.**—Of the symptoms, the *headache, chilliness, malaise,* general pains and the fever may be safely ascribed to the systemic effects of an infection. The stuffy feeling in the head, *mouth breathing,* nasal tones, loss of the sense of smell, and inability to perceive flavors are all due to the swollen, œdematous condition of the mucosa and the engorgement of the submucosa—this sometimes amounts to complete obstruction. Sneezing results from irritation of the nasal mucous membrane; hence, in this case, must be due to direct action of the infectious organism or the beginning inflammation on the nerve endings of the mucosa. As the inflammatory conditions arise there is a lessened nutrition of the mucosa and degeneration, desquamation, and discharge results. The mucous glands pour out an increased amount of secretion, which carries with it the cells from the mucosa pus cells and various micro-organisms. The inflammation often extends to the frontal and ethmoidal cavities, the antrum, and the middle ear, causing symptoms arising from congestion, degeneration, and even desquamation of the mucus lining those cavities.

The pharynx and larynx are frequently involved, the extent of involvement depending upon (*a*) an extension of the infection and (*b*) impairment of nasal functions—viz., warming and filtering the air. If pharyngitis occurs, the sore throat and sneezing are due to catarrhal inflammation, as in the previous disease.

b. Chronic Coryza, or Rhinitis.

1. **Pathology.**—Chronic nasal catarrh is characterized by a variety of pathologic states, all of which have a definite relationship, one being the sequel of another. The mucosa may show the same changes as in the acute form. These conditions persisting indefinitely, result in a hyperplasma, or the formation of new tissue; if this progresses to a certain degree, the nutrition is cut off and the death of the tissue results; if it is local, polypi may result.

2. **Symptomatology.**—The symptoms lack the features of infection. They are generally vague and consist of increased susceptibility to acute attacks, stuffy feeling in the head, mouth breathing, loss of the sense of smell and perception of flavors; if ulceration occurs, an offensive discharge is common.

3. **Physiology.**—The explanation of the above symptoms has been considered in connection with the acute disease; polypi may cause complete nasal obstruction.

2. PHARYNGITIS AND TONSILLITIS.

a. Acute.

The pharynx and tonsils are so frequently diseased at the same time that they will be considered in this connection under one head: strictly speaking, they might with equal or greater propriety be considered under diseases of the digestive tract.

1. **Pathology.**—The mucosa of the pharynx is congested and swollen; the tonsils look red and inflamed, are enlarged, and densely infiltrated with white blood cells, some red, and uncertain quantities of serum and fibrin. The crypts may be filled with an exudate and abscess formation in the tonsillar stroma may occur. The adjacent cervical lymph glands may show inflammatory enlargement.

2. **Symptomatology.**—Headache, chill, and fever are present if infection is the etiologic factor in the production of the disease. Other symptoms are soreness, dryness and tickling of the throat, and stiffness of the neck.

3. **Physiology.**—As suggested in the preceding paragraph, the chill, fever, and headache are due to infection. The soreness and tickling are due to irritation of pharyngeal and tonsillar nerve endings, while the stiff neck and painful cervical glands evidence the activity of the lymphatic glands in their effort to destroy the infection.

b. Chronic.

1. **Pathology.**—These diseases may result from any of the following conditions: relaxed mucosa, dilated vessels, proliferation and even

hypertrophy and hyperplasia of the pharyngeal and tonsillar lymphoid tissue.

2. **Symptomatology.**—The symptoms arising from an uncomplicated case of chronic pharyngitis are scarcely noticeable. There may be mouth breathing, an offensive pharyngeal discharge, and impaired hearing. Chronic tonsillitis frequently displays no symptoms of note, merely a sense of fulness and obstruction. The chronic condition predisposes to acute attacks in both pharyngitis and tonsillitis.

3. **Physiology.**—In pharyngitis the mouth breathing results from proliferation of the lymphoid tissue in the vault of the pharynx: these proliferations are commonly called adenoids. The secretion is the result of the pharyngeal inflammation. Loss of hearing results from an extension of the inflammation to the Eustachian tubes.

3. LARYNGITIS.

a. Acute.

1. **Pathology.**—The next pathologic condition to which attention will be called is found in acute catarrhal laryngitis. In this disease the mucous membrane of the larynx and contiguous structures is swollen and œdematous; the vocal cords are red, lustreless, and thickened, and a mucous layer covers the whole affected area.

2. **Symptomatology.**—Symptoms of this disease vary greatly, according with the intensity of the attack. There may be no constitutional symptoms: if present, they arise from the infection, which, though not proven, is assumed. Others are: (I) tickling of the throat, (II) cough, (III) sore throat, (IV) changed voice or loss of voice, and (V) dyspnœa.

3. **Physiology.**—The tickling and *soreness of the throat* and the *cough* are due solely to irritation of the laryngeal nerve endings. The changes in the voice are the result of thickening and infiltration of the vocal cords: this interferes with proper vibratory activity. Dyspnœa is a symptom which may be entirely absent, or it may become the symptom of importance. When it does appear it results from a more or less pronounced narrowing of the laryngeal passage, this narrowing being caused either (I) by œdema or (II) by spasm.

b. Chronic.

1. **Pathology.**—The chronic lesions of the larynx are a result either of repeated attacks of acute laryngitis, of tuberculosis, or of syphilis; hence very diverse pathologic findings are the rule. In the first form, mere swelling of the mucous membrane constitutes the principal change. In tuberculous laryngitis there is a primary inflammation which soon shows the characteristic tubercle formation, coalescence,

caseation, and ulceration. Syphilitic laryngitis may show only mild mucous-membrane ulcers, or gummata, which result in very deep destructive ulcers, extending into the submucosa and producing great deformities where the scar tissue contracts.

2. **Symptomatology.**—In all the above conditions there are changes in the voice, amounting sometimes to a complete loss of phonation: tickling and cough also are common. In tuberculous forms dysphagia is common, and in this as in the syphilitic form œdema may supervene and prove fatal. The only characteristic symptoms of syphilitic laryngitis are those of obstruction or loss of function of the epiglottis.

3. **Physiology.**—The *changes in the voice* are due to thickening of the mucosa covering the vocal cords or *infiltrating changes* affecting their vibratory functions. The tickling and cough are due to irritation. Dysphagia is due to deep ulceration in the lower pharynx and in the epiglottis; as a consequence, muscular action, which is necessary to swallowing, becomes very painful when the ulcers are disturbed by it. The deep scars of syphilitic laryngitis deform and injure according to their size and location, and upon these factors depend the character and intensity of the symptoms.

4. BRONCHITIS.

a. Acute.

1. **Pathology.**—An acute inflammation involving the nares, pharynx, and larynx is prone to extend downward and become an acute bronchitis. The gross pathology of this disease is (I) a thickened, reddened mucosa of the trachea and bronchi, and a mucous or mucopurulent exudate. Microscopically, there is infiltration, degeneration, and desquamation of the mucosa, accompanied by (II) a lack of secretion, (III) then a profuse secretion from the glands of the submucosa. This makes the exudate consist of mucus, red and white blood cells, desquamated cells (ciliated and glandular), and bacteria.

2. **Symptomatology.**—The symptoms are usually ushered in by nasal, pharyngeal, and laryngeal inflammation, with the symptomatology noted above. When the inflammation reaches the trachea and bronchi, the following additional symptomatology may be observed: (IV) a feeling of rawness and unusual sensitiveness beneath the sternum; (V) an ill-defined sensory disturbance, resulting in a feeling of compression and soreness in the chest walls; (VI) a dry, ringing, unproductive, paroxysmal cough, and sometimes (VII) dyspnœa. Soon the coughing is attended by an expectorate of varying character and amount, and if, uncomplicated, the disagreeable symptoms decline.

3. **Physiology.**—As in the preceding diseases, any *constitutional disturbances* will be ascribed to infection. Cough is the result of tracheal and bronchial inflammation, which irritates the vagi nerve endings of the mucosa. The *dryness* and *congestion* of the *mucous membrane*, together with the hypersensitiveness of the nerve endings, will be assumed as causing the substernal soreness; while the violent muscular efforts exhibited in the cough cause the sore feeling in the chest wall. The sputum or secretion arises from the exudative and degenerative processes mentioned above. Dyspnœa is not a marked symptom, and, if present, is a fairly certain indication that the disease is extending into the finer bronchi—in fact, that the process is becoming a bronchopneumonia.

b. Chronic.

1. **Pathology.**—The pathology of chronic bronchitis is exceedingly varied. The mucosa and submucosa may show all the changes due to chronic inflammation; first there may be an infiltration, and this may be followed by a uniform hypertrophy; there may be granular outgrowths, atrophy, desquamation, and ulceration. Dilatation of air cells and bronchioles occurs if the disease persists.

2. **Symptomatology.**—In uncomplicated cases a chronic cough, varying in intensity with the season, especially marked in winter, and a sputum which is not characteristic are the only symptoms. However, since this disease is frequently associated with cardiac and renal diseases, and is attended by emphysema and bronchiectasis, shortness of breath and other symptoms of poor aeration of the blood are quite common.

3. **Physiology.**—The changes in the mucosa result in irritation, by which a cough is produced; reflexly, the presence of secretion and the inability of the ciliated cells to remove it also irritates and may help to cause the cough.

5. BRONCHOPNEUMONIA.

The above disease is so closely related to bronchopneumonia, in fact so frequently precedes it in a clinical picture, that a few paragraphs regarding pathology and symptomatology of this very serious disease cannot be considered amiss in this connection.

1. **Pathology.**—A typical bronchopneumonia has the following pathologic findings: Macroscopically, there are to be found solid nodules, these varying in size and numbers; each nodule represents the lung area supplied with air by a single bronchus; hence the size of the nodule depends upon the size of the bronchus involved and the depth to which the adjacent tissue is affected by inflammation. Microscopically, these nodular areas show the involved alveoli and bron-

chioles filled with the products of catarrhal inflammation—serum, desquamated epithelium, red and white blood cells, fibrin, and bacteria—all varying as to quantity in individual cases and different stages of the disease; there is also interstitial engorgement and infiltration with leukocytes, and even red blood cells.

2. **Symptomatology.**—The disease may be ushered in by symptoms of an acute infection, or complicating some other disease one will notice an irritating dry cough increasing in intensity, fever, rapid pulse, rapid respiration, and thoracic tenderness; then dyspnœa and even asphyxia may supervene and a fatal termination ensue, though this is by no means the usual result.

3. **Physiology.**—Taking up the symptoms in order: Cough results reflexly from irritation of the terminal filaments of the vagi, the irritation being due to inflammatory changes in the mucosa and the engorgement of the submucosa. The fever and rapid pulse are due to toxæmia, which is partly but not wholly responsible for rapid respiration. In every bronchopneumonia there are many of the consolidated areas previously mentioned, and each one represents a certain amount of lung tissue surrounding each nodule relatively inactive; hence the rapid breathing and subsequent dyspnœa are due in great part to deficient aeration of the blood. Some of the nodules may lie close to the pleural surface of the lung and involve the pleuræ, resulting usually in granular roughening of the visceral layer, though this condition may become more marked and result in adhesion forming between the two layers. These inflamed areas on the pleuræ cause the sharp stitch-like *pain in the side,* and localized thoracic tenderness which is so marked in some cases. When such a pathologic condition is present it undoubtedly modifies the character, if not the rate, of respiration. The violent paroxysmal cough is another marked factor in producing sore and tender chest walls—this from strain and spasmodic contraction of the expiratory muscles.

6. LOBAR PNEUMONIA.

1. **Pathology.**—This disease is due to an infection, is, in fact, one of the most characteristic of infectious diseases, and has fairly typical pathologic findings. In addition to the presence of bacteria in the blood, lungs, in fact almost anywhere in the body, the disease is characterized by an exudative inflammation of the alveoli and bronchi of one or more lobes of the lungs; the exudate being composed of bacteria, serum, red and white blood cells, and alveolar epithelium, all in various stages of degeneration. The exudate differs in composition in the different stages of the disease, and in resolution is disposed of either by liquefaction and absorption or expectoration.

2. **Symptomatology.**—The classic symptoms are: chill, fever, rapid pulse, flushed face, headache, general pains, respiration very rapid

and shallow, cough, pain in the side, bloody sputum, dyspnœa, delirium, and, in a typical recovery, a crisis.

3. **Physiology.**—In this disease are found more marked than in almost any other the symptoms of an acute infection—viz., chills, fever, rapid pulse and respiration, general pains, headache, and even delirium, and in this connection it will be well to consider these symptoms in order. The most generally accepted theory is that they are the result of a toxæmia acting upon the central nervous system, affecting the different centres, first by stimulating and later—if the stimulation is long continued—depressing and paralyzing them. The chill, then, may be explained as being the result of toxic stimulation of the centres governing the vasoconstrictors of the skin, and this stimulation, if long continued, would bring about a paralysis of these centres, and cause a flushing of the face, which is very common.

Fever is a term applied to any condition in which the body temperature ranges above normal. It is probably the result of a toxæmia, this acting either by causing vasomotor disturbances, deranging the centres which control heat production and dissipation, or by interfering with metabolism in the blood stream and tissues. Pneumonia is a disease which very strongly supports the theory that toxæmia is the cause of fever, since at the crisis, when the toxins are overcome and their elimination begins, the fever almost entirely disappears. *The headache, general pains, delirium, rapid pulse,* and, in part, the rapid rate of respiration, are due to the action of toxins upon the various centres in the cerebrum and medulla; headache, general pains, and delirium being probable results of congestion brought about by vasomotor paralysis, the others being due to either direct action on the various centres or to circulatory disturbances not fully understood. There are more symptoms due to local conditions, as pain in the side, more marked and constant than in bronchopneumonia, but due to the same cause, pleurisy. Cough, a reflex result of laryngeal and bronchial irritation; that part of the increase in respiratory rate which remains after the crisis, due to improper aeration of the blood in the congested exudate-filled lobe or lobes; the characteristic sputum which comes from capillary hemorrhage, and exudate of serum, fibrin, blood cells and their degeneration.

7. INFLUENZA.

Influenza follows the type of acute specific infections, and if the local lesions occur in the respiratory tract, as is common but not universal, any symptoms from those of a coryza to a pneumonia may be observed as the process attacks one structure after another. There is nothing peculiar about an attack of influenza, except the severity of the constitutional symptoms in comparison with the pathologic changes and physical signs, and this peculiarity must result from the intensity of the toxæmia.

8. MILIARY TUBERCULOSIS.

Acute miliary tuberculosis is more a circulatory than a respiratory disease; hence will not be considered in this connection. It is really a general infection with the tubercle bacilli, resulting in (I) a profound toxæmia, and (II) characteristic tuberculous lesions in various parts of the body, where the bacteria are deposited by the blood stream.

9. PULMONARY TUBERCULOSIS.

a. Acute.

Pulmonary tuberculosis of the acute type is usually pneumonic or bronchopneumonic in character, and cannot be differentiated from those diseases in the early stages. It is only the protracted course and discovery of the tubercle bacilli which make the diagnosis possible. Hence, the symptomatology need not be discussed here, as it has been presented under the above diseases.

b. Chronic.

1. **Pathology.**—The pathology is varied and consists in the formation of tubercles: these undergo softening; then they coalesce, ulcerate, and form cavities.

2. **Symptomatology.**—The symptoms are not stereotyped, but may be summed up as comprising general debility, hemorrhages, fever, cough, sputum, and dyspnœa.

3. **Physiology.**—The poisons secreted by the tubercle bacilli are responsible for the general loss of health and fever; hemorrhage is due to ulceration into a bloodvessel; cough results from bronchial irritation. The sputum comes from the breaking down of tubercles, the accompanying mixed infection, and the chronic inflammation which surrounds the tuberculous area. Dyspnœa is here, as elsewhere, a sign of deficient aeration of the blood.

10. PLEURISY.

Pleurisy is a term applied to acute and chronic inflammations of the membrane lining the pleural cavities.

1. **Pathology.**—There is no typical pathology. The pleural surfaces may show a granular roughening, there may be adhesions

between the parietal and visceral layers, or there may be a very marked serous effusion. Whatever the final picture be, the initial changes are probably the same—viz., engorgement of the pleural capillaries, exudation of white and red blood cells, serum, and fibrin through the capillary walls and pleural membrane, these changes so affecting the pleural endothelium that it either becomes roughened or desquamates.

2. **Symptomatology.**—The symptoms are generally chill, fever, sharp and lancinating pain in the side, cough, a varying amount of sputum, and sometimes dyspnœa.

3. **Physiology.**—The chill, fever, etc., suggest that infection is responsible for the disease, though these may come from associated or preceding pulmonary lesions. The roughening of the pleural membrane and the beginning adhesions are pathologic conditions which seem to be most clearly responsible for the *pain in the side* and, in part, for the cough. Either the loss of the pleural endothelium exposes the nerve endings to irritation by friction when respiratory movements occur, or the pleural inflammation makes the nerve endings more easily irritated by motion. It is certain that the respiratory movements aggravate both the pain and the cough, since both these symptoms are greatly relieved by immobilizing the affected side. This therapeutic test supports the above theory—viz., that roughening and desquamation of the pleural cells increases the irritability of the nerve endings and renders the otherwise painless gliding of the pleural membranes on each other a very painful operation, so painful that the character and rate of respiration may be greatly influenced by it in a reflex manner. The *cough*, which may be very irritating, is here, as in other diseases, a reflex manifestation of nerve irritation: whether this irritation is pleural, subpleural, or bronchial is not certain, and its location may vary with the causes which brought on the pleuritic condition: that is, whether tuberculous or pneumonic.

The *sputum* is of varying character, depending more upon coincident or preceding conditions in the lung than upon pleural pathology.

Dyspnœa is the result of a number of conditions. It may result from the reflex muscular spasm which, in a manner, immobilizes one side of the chest and reduces the available lung space to practically one-half of normal; it may be due to extensive adhesions which render complete inspiration and expiration impossible, or it may come from an extensive serous exudate which compresses the lungs and reduces the amount of tidal air which can enter the lungs during each inspiration.

11. ASTHMA.

1. **Pathology.**—Bronchial asthma is generally admitted to be a neurotic affection characterized probably by a spasm of the bronchial muscularis, a simultaneous hyperæmia or œdema of the mucosa, and a peculiar exudate of mucin. Absolute knowledge of the morbid anatomy is wanting.

2. **Symptomatology.**—The symptoms are very sudden in onset: The patient lacks air, breathing becomes labored, and an expiratory dyspnœa supervenes; a dry, tight cough, accompanied by the characteristic asthmatic sputum, now appears, and cyanosis may be marked.

3. **Physiology.**—In view of the uncertain pathology of this disease, much must be assumed of its physiology. It seems that there must be some irritant or irritants which, under certain conditions, are capable of exciting powerful reflex contractions of the muscular walls of the bronchi. Since inspiration is more powerful than expiration, the bronchial contraction really increases the amount of air in the alveoli, causing emphysema and increased expiratory effort or expiratory dyspnœa.

The cough and sputum result from the concomitant bronchiolitis.

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B. GASTRIC DIGESTION.

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  (2) *Diminished Hypochlorhydria and Anachlorhydria.*
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DIGESTION. INTRODUCTION.

A. THE COMPARATIVE PHYSIOLOGY OF DIGESTION.

1. INTRACELLULAR DIGESTION.

In the nature of the case an organism which consists of only one cell must take in nutriment through the ectosarc or exoplasm into the endosarc or endoplasm of the cell. If the nutriment be fluid, the absorption is a simple process, influenced largely by the physical laws of osmosis, and may be followed by a rapid assimilation of the absorbed nutriment. If the nutriment be solid, the process of taking it through the ectosarc is a mechanical one, and is accomplished by movements of the protoplasm. Once the solid particle of food is engulfed in the endosarc, a true process of digestion or solution is necessary before the nutriment may be assimilated or built up into cell protoplasm. For a brief description of the whole process of nutrition, including digestion, in the unicellular animals, particularly the amœba, the reader is referred to *General Physiology* (p. 42). The digestion in unicellular animals is necessarily of the intracellular type. *The Cœlenterates* afford an example of a type of animal in which a definite tissue is set apart for the function of digestion. This specialized tissue, the entoderm, lines a cavity or a more or less complex series of cavities formed by an invagination or dipping in surface of the developing organism. Solid nutriment taken :se cavities is taken up by the entodermal cells which line the and digested within them. The product of digestion is in ssed on to the non-digesting tissues by diffusion or by circula- ough the *gastrovascular canals.* Among the cœlenterates at ıe form has been discovered—"the fresh-water medusa—in he cells which line the mouth of the gastric tube have the ı of secreting a digestive fluid." (Lankester.) But this cœlen- :tains the primitive intracellular method of digestion through- greater part of the gastric tube.

2. DIGESTION BY SECRETED FERMENTS.

:ransition from the primitive to the higher mode of digestion dual one. The lowest worms—Turbellaria—have the intra- mode, and the mesoblastic cells of echinoderm larvæ manifest ıe property. In this connection one recalls also the intra- digestion of bacteria, etc., by the leukocytes of the higher .

:rtebrates and the higher invertebrates possess an alimentary ırough which the food passes while being acted upon by ferments which produce a progressive series of digestive . This canal is usually differentiated into several distinct ;, in which particular steps of the process are performed. arly part of the process the food is triturated. Either before, or after trituration it is softened and lubricated by secretion ılimentary canal. The food is passed along the canal by altic motion of involuntary muscles within the wall of the

ırocesses described in the above paragraph are all mechanical The food for the higher animals is for the most part solid. e liquid food is not usually in a condition that permits imme- ısorption. It must be changed chemically. The insoluble , proteins, and fats must be changed to soluble and diffusible ɔeptones, and soaps. But the mass of material is too great ıanged by the cells lining the alimentary canal; so nature :loped a specialized method to fit the conditions: (I) Special- reting cells grouped into glands form ferments or enzymes ıey pour through ducts into the alimentary canal. (II) The enzymes induce extensive chemical changes in the foods, ; them all finally to diffusible solutions.

wo kinds of digestion are, then, *intracellular* and *extracellular;* : affected through the agency of ferment action, but in one ferments act on foods taken into cells and in the other ı not yet absorbed.

B. ANATOMIC INTRODUCTION.

1. A SUMMARY OF THE ANATOMY OF THE DIGESTIVE SYSTEM.

a. The System in General.

(*a*) **The Digestive System** consists of the *alimentary canal*, together with certain *glands* whose ducts open into the canal.

(*b*) **The Alimentary Canal** begins with the mouth and ends with the anus. It consists of: (*a*) the oral cavity; (*b*) the pharyngeal cavity; (*c*) œsophagus; (*d*) stomach; (*e*) small intestine, composed of duodenum, jejunum, and ileum; (*f*) large intestine, composed of cæcum, colon, and rectum.

(*c*) **The Tube** is lined throughout with mucous membrane, outside of which is a submucous coat. Both of these coats vary much in different portions of the tube. The mucous epithelium of the mouth and œsophagus is stratified, while that of the stomach and intestines is simple columnar. The glands of the mucosa are variously modified in different parts of the canal. The submucosa is thin in the mouth and pharynx, but abundant in all other parts of the tracts.

(*d*) **The Wall of the Free Tube**—from the beginning of the œsophagus to the anus—contains muscular coats, covered externally with a fibrous coat. All of that portion of the canal within the abdominal cavity receives an outer peritoneal investment.

(*e*) **A Typical Portion** of the wall of the alimentary canal consists of: (I) *Mucous membrane*, whose epithelium is the *secreting* and *absorbing* portion of the wall. (II) *Submucous coat*, whose loose fibrous structure permits free folding and free movement of the mucosa, and furnishes a favorable course for bloodvessels, lymphatics, and nerves. (III) *Muscular coat*, whose two or three layers of involuntary muscle tissue perform the slow peristaltic contractions which are so important a factor in digestion. (IV) *Fibrous coat*, which lends additional strength to the walls of the tube. Usually included with this coat is the pavement epithelium of the peritoneum.

(*f*) **The Epithelium of the Mucous Membrane** is hypoblastic in origin, except in the mouth, upper pharynx, and lower rectum. The serous epithelium of the peritoneal covering of the tube is from the *splanchnopleuric mesoblast*. All of the structures between these two epithelial boundaries (nerve tissue excepted) represent *mesenchymic mesoblast*. The nerves invade these tissues from the *neural epiblast*.

(*g*) **Upon the Inner Surface** of the mucous lining innumerable glands open. These glands are developed in the embryo by evagination from the mucous surface; the gland epithelium has, therefore, the same histogenesis as the mucous epithelium from which it evaginated; the epithelium of all glands opening into the mouth being epiblastic, and that of all glands opening in the stomach, for example, being hypoblastic.

(*h*) **A Large Proportion of these Glands** are mucus-secreting glands. In certain locations the glands present both structural and functional modifications; in the stomach the peptic glands present, structurally, the striking parietal or acid cells; while, functionally, these glands secrete both pepsin and hydrochloric acid.

FIG. 153

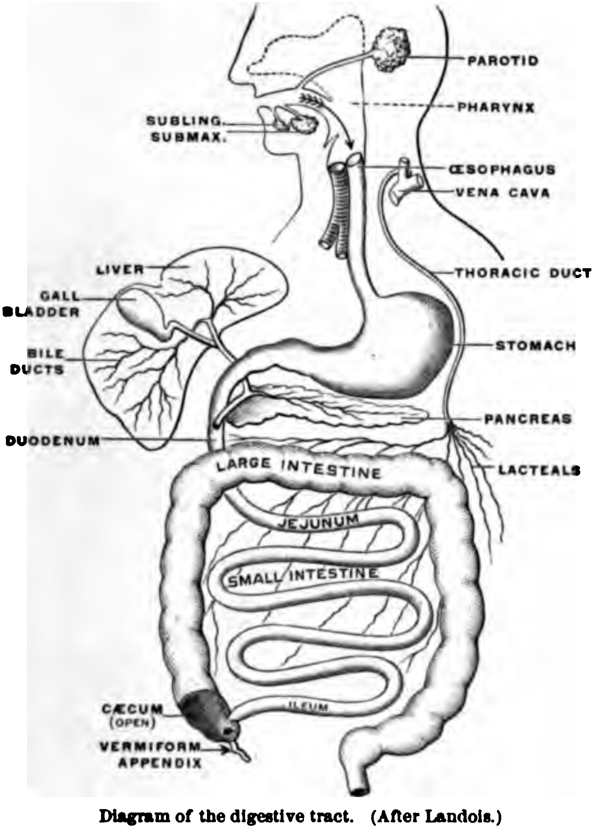


Diagram of the digestive tract. (After Landois.)

(*j*) **Besides these Glands within the Walls** of the canal there are several large glands—salivary glands and pancreas—which lie quite outside the wall of the canal, and pour their secretion into the canal through a duct whose epithelial lining is continuous with the epithelium of the canal. The active cells of these glands are modified epithelial cells, and with the lining of the duct are derived, in the embryo, by evagination from the lining of the alimentary canal.

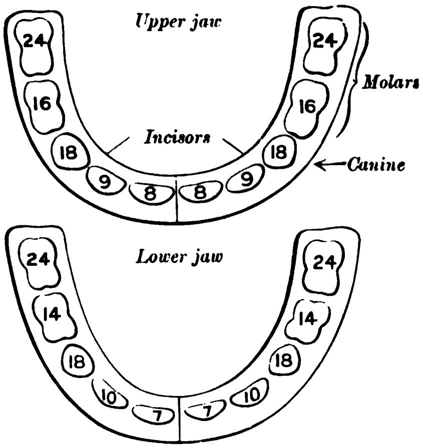
b. Particular Segments of the Tracts.

1. **The Oral Cavity.**—This portion of the alimentary canal is especially adapted, by its firm stratified epithelium, to receive solid food. The skeletal and muscular structures which surround this cavity perform important parts in its functions. The skeletal portion of the roof of the cavity is formed by the superior maxillary bone, presenting the palatal plate and the alveolar ridge; while the skeletal portion of the floor of the cavity is formed by the inferior maxillary bone, presenting an alveolar ridge. These alveolar ridges are armed with teeth, which are set in bony sockets lined with periosteum.

(*a*) **The Teeth.**—For a description of the minute structure of the teeth, the reader is referred to any work on histology. There are two sets of teeth, a *temporary* set and a *permanent* set. The time of eruption is important to the physiologist, because it is indicative of the kind of food which the organism requires. The time of *eruption* of the *teeth* is shown in Figs. 154 and 156.

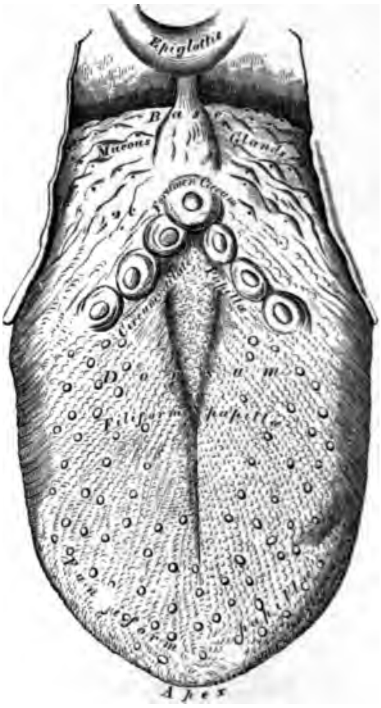
(*b*) **The Muscles of Mastication** are those which produce the movements of the inferior maxillary bone, especially the temporals, the masseter, the pterygoid; also those which produce movements of the cheeks and tongue.

FIG. 154



Temporary teeth. (Time given in months.)

FIG. 155



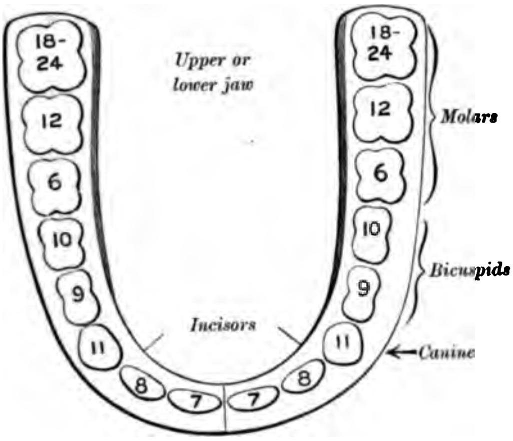
The tongue.

(*c*) **The Glands of the Mouth** are the numerous mucous glands whose function is to keep the mouth moist, also the highly developed *salivary glands.* There are three pairs of salivary glands—the submaxillary, the sublingual, and the parotid. (For figures see Secretion.)

(*d*) **The Tongue** lies in the floor of the mouth, and is composed mainly of longitudinal and transverse muscle fibres, through whose combined action the tongue may be retracted, protruded, raised, lowered, or circumducted.

This organ is most useful in *mastication.* In some animals it is used as an organ of *prehension.* In most animals it is used as a *tactile* organ. In the mucous membrane of the tongue are located the principal end organs of the *sense of taste.* Especially adapting the surface of the tongue for these various functions are the papillæ, which are of three varieties: (I) the circumvallate, (II) the fungiform, and (III) the conical. The first two forms named contain taste buds. (See Fig. 157.) (For other figures see Taste.)

FIG. 156



Permanent teeth. (Time given in years.)

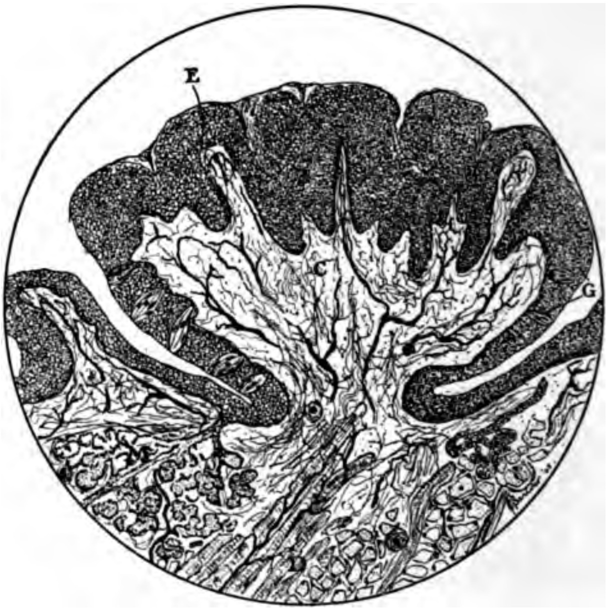
2. **The Pharynx.**—The uvula marks the boundary between the oral cavity and the pharynx. This cavity is common to the digestive and respiratory systems. The portion of it which is concerned in swallowing is lined with stratified epithelium, and is supplied with mucous glands. Its walls contain three sets of muscles (*Pharyngeal constrictors*) whose contraction aids in deglutition.

3. **The Œsophagus.**—This is the tube which leads from the pharynx through the thorax to the stomach. It possesses the four typical coats described above. The mucous membrane presents longitudinal folds, and its epithelium is stratified. The numerous mucous glands dip down into the submucosa. The two heavy muscular coats serve the function of deglutition.

4. **The Stomach.**—This very important viscus is a dilatation of the alimentary canal. It has the four typical coats; mucosa, sub-

mucosa, muscular, and fibrous. It is the first portion of the canal within the abdominal cavity, and is, therefore, the first to have a peritoneal investment. The mucosa is provided with two varieties of glands (peptic and pyloric), which will be described under Gastric Digestion. This coat lies in prominent folds or *rugæ* upon the subjacent tissues. The muscular coat consists of two principal layers of involuntary muscle, an inner circular and an outer longitudinal layer, while an imperfect oblique layer may be found at the cardiac end. The orifice between the œsophagus and the stomach is called

FIG. 157



Section of circumvallate papilla: *E*, epithelium; *G*, taste buds; *C*, corium with injected bloodvessels; *D*, cross and longitudinal muscle fibres; *M*, gland with duct. (Barlow.)

FIG. 158

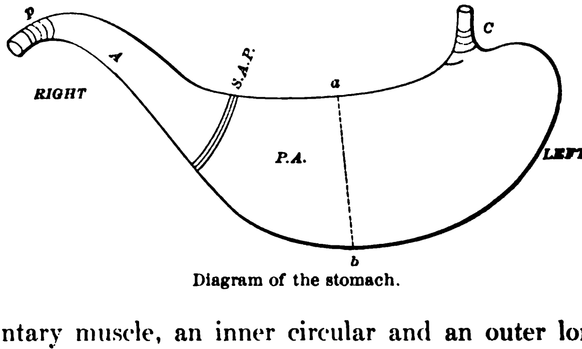
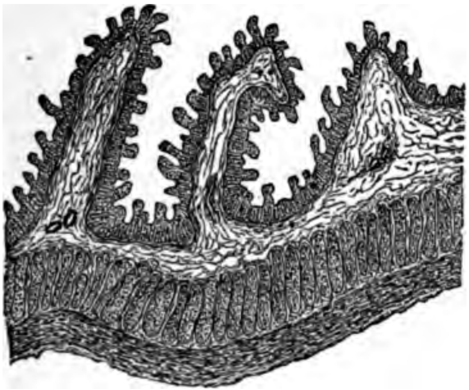


Diagram of the stomach.

the *Cardia* (Fig. 158, *C*). It is guarded by a sphincter. The orifice between the stomach and duodenum is called the *Pylorus* (158, *p*). It is also guarded by a sphincter. At a point about two-thirds of the distance from the cardia to the pylorus is a band of especially strong circular muscles. This has been called by Hofmeister and Schutz the "Sphincter antri pylorici" (Fig. 158, *S. A. P.*). The portion of the stomach between this sphincter and the pylorus is called the *Antrum* (*A*). The middle third of the stomach is called the *preantral* segment (*P. A.*) The antral and preantral segments together make the *pyloric portion*, while the segment nearest the cardia is called the *cardiac portion*. The use of these terms will be necessary in the description of the movements of the stomach.

FIG. 159



Longitudinal section of human small intestine, showing general relation of the folds constituting the valvulæ conniventes to the mucosa and submucous coat; the latter contributes the fibrous core over which the mucosa with its villi and glands extend. (After Piersol.)

5. **The Small Intestine.**—This is a tube of fairly equal calibre lying in coils in the abdominal cavity. It is sixteen to twenty feet in length, and passes into the cæcum through the ileocæcal valve. It is subdivided into three portions—the duodenum, jejunum, and ileum. The four coats of the small intestine differ from those of the stomach principally in the variations of the mucous membrane. The folds of the latter are transverse and are called *Valvulæ conniventes.* (See Fig. 159.)

The mucous membrane presents two important features: (I) the villi, which are finger-like projections into the lumen of the intestine; (II) the crypts of Lieberkühn, which dip down from the general surface of the mucosa to the muscularis mucosa. The crypts will be described under Digestion and the villi under Absorption; (III) the glands of Brunner in the submucosa of the duodenum.

Tributary to the duodenum are two most important glandular bodies, the pancreas and the liver. As the latter has little to do with digestion and much to do with metabolism, it will be described in the chapter on Metabolism. The *pancreas* is a tubuloracemose gland, resembling the salivary glands, except that the alveoli are tubular.

Fig. 160

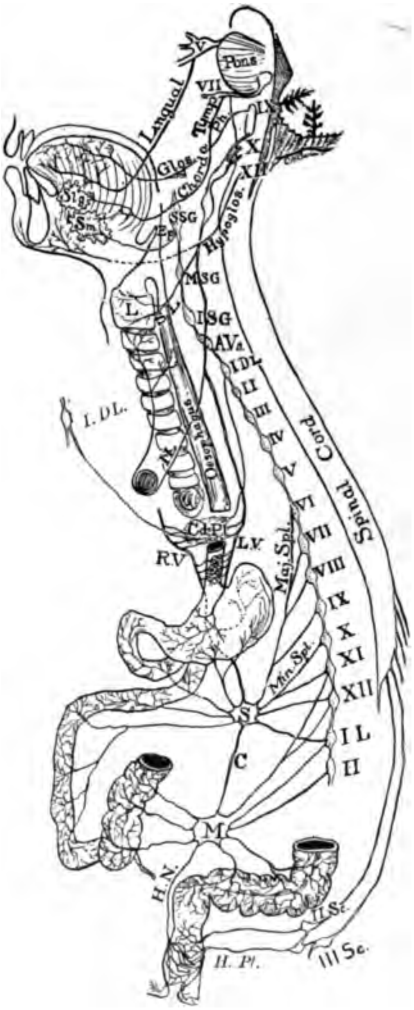


Diagram showing the innervation of the digestive system.

VII.	Seventh cranial nerve.
V.	Fifth cranial nerve. (Gasserian ganglion.)
IX.	Ninth cranial nerve.
X.	Tenth cranial nerve.
XII.	Twelfth cranial nerve.
Slg.	Sublingual gland.
Sm.	Submaxillary gland.
S. S. G.	Superior sympathetic ganglion.
M. S. G.	Middle sympathetic ganglion.
I. S. G.	Inferior sympathetic ganglion.
Ep.	Epiglottis.
I. DL.	First dorsal sympathetic ganglion.
II. to *XII. DL.*	Second to twelfth dorsal sympathetic ganglion.
I. L. and *II. L.*	First and second lumbar sympathetic ganglion.
S.	Solar plexus.
Min. Spl.	Minor splanchnic nerve.
Maj.	Major.
Cd. Pl.	Cardiac plexus.
II. Sc.	Second sacral sympathetic ganglion.
III. Sc.	Third sacral sympathetic ganglion.
R. V.	Right vagus nerve.
L. V.	Left vagus nerve.
L.	Larynx.
I. L.	Inferior laryngeal nerve.
S. L.	Superior laryngeal nerve.
H. N.	Hypogastric nerve.
H. Pl.	Hemorrhoidal plexus.
I. DL.	First dorsal sympathetic ganglion, left and right.
M.	Mesenteric plexus.
C.	Communicating branch.
A. Vs.	Annulus of Vieussens.

The secreting epithelium of the pancreas is hypoblastic in origin, being derived from the primitive midgut by evagination.

6. **The Large Intestine.**—This portion of the intestine consists of the cæcum with its vermiform appendix, the capacious and transversely constricted colon, and the rectum. The structure of the walls

is quite similar to that of the small intestine, except that there are *no villi*, and the tubular glands differ from the crypts of Lieberkühn in having a greater proportion of the mucus-secreting goblet cells.

C. SECRETION.

1. GENERAL CONSIDERATIONS.

The tissue activity of the organism may be conveniently divided into three groups:

(α) MUSCULAR ACTIVITY, the general function of muscular tissue, manifesting itself in motion and heat; (β) NERVOUS ACTIVITY, the general function of the nervous tissue, including all nervous acts from sensation to reason; (γ) GLANDULAR ACTIVITY, the general function of epithelial and lymphoid tissue, including all of those metabolic changes which result in the elaboration of a special mixture, either (I) by separating (*selecting*) out of the liquids of the body compounds which already exist, forming of these a new combination for a special purpose; or, (II) by actually *forming* new substances which may be combined with selected or separated substances to make a special mixture. Of these forms of glandular activity one may cite numerous examples: (I) the elaboration of lymph, urine, perspiration; (II) gastric juice, pancreatic juice, saliva, bile, synovial fluid, lacrymal fluid, sebaceous matter, milk, etc. If one classifies as glandular all those tissues which possess the power of elaboration by *selection* or *formation*, he will find that he has included practically the whole of the derivatives of the hypoblast, special portions of the epiblast, the whole of the derivatives of the splanchnopleure and somatopleure, together with the mesoblastic epithelium of the genitourinary system, and the mesoblastic lymphoid tissue. There seems to be no doubt that all of the tissues enumerated possess this power to a greater or less extent. The glandular activity of the hypoblastic epithelium is specialized in such organs as the pancreas and liver, and such specialized portions of the mucous membrane as the gastric and enteric glands. But the whole epithelium contains a large proportion of the mucus-secreting goblet cells; some writers stating that any cell of the mucous membrane may become a goblet cell, secrete its mucus, and resume its original form as a columnar epithelial cell.

Even absorption of the products of digestion from the alimentary canal is not a simple diffusion and filtration, but is attended with a marked activity of the epithelium; first, in a certain degree of selection, second, in a partial elaboration, changing the peptone to a higher proteid form before it is passed into the capillaries of the portal system, also changing fatty acids and glycerin to fat. That portion of the epiblast which lines the mucous openings of the body—*i. e.*, mouth, nose, anus, and urethra—and such mucous surfaces as the vulva, prepuce, and conjunctiva are richly supplied with mucous glands; but the goblet cells are absent from all of these locations except the respiratory region of the nasal mucous membrane. In that portion of the epiblast which covers the general surface of the body the glandular activity is subordinated to the function of protection. There are innumerable sebaceous glands and sweat glands, but the general surface cannot be called a glandular one.

The endothelial lining of all serous cavities is now conceded to have a general glandular activity. The serous fluid which occupies these cavities is not identical with blood plasma, and though an increased venous pressure leads to an increase of the volume of lymph and serum, these fluids differ quantitatively from plasma. Such a difference cannot be accounted for by purely physical laws of filtration and diffusion; there must be a selective activity on the part of the endothelial tissues. This selective activity manifested by endothelial tissue in general justifies its classification among glandular tissues. However, clinical experience indicates that the proportions of salt are only slightly changed, if at all, and that changes in specific gravity are due almost wholly to variation of the albumin content.

In the same category belongs the endothelium of the circulatory system; though glandular activity has been demonstrated only in the endothelium of capillaries and lymph radicals. The genito-urinary system furnishes numerous examples of glandular activity: the ovary and testes, and the genital ducts and canals, including the oviduct, uterus, vagina, vas deferens, seminal vesicles, the prostate, and the kidney. The epithelial tissues of all of the organs enumerated are glandular tissues. It is to be noted here that the secretion of the genital glands is largely composed of cellular elements; the same may be said of the lymphoid tissues of the circulatory system, and of the preliminary secretion (colostrum) of the mammary glands.

2. SECRETION DEFINED.

The term *secretion* may be defined as the special activity of the glandular tissues, or, better, the elaboration of fluid or semifluid mixtures by selection from the fluids which surround the active cells or by formation from materials within the active cells. In the secretion of the gastric juice the water and the inorganic salts are selected from the tissue plasma which bathes the glandular epithelium; the hydrochloric acid is *formed*, probably, by a reaction between salts of the plasma. It is necessary, however, that these salts be taken into the secreting epithelium and brought under the influence of special forces in order that the reaction may take place. The pepsin of the gastric juice is *formed* from the protoplasm as a product of cell metabolism.

The term secretion in its most general application may be applied to the part which the epithelial cells take in modifying the fluids which filter and diffuse through them. That the absorbing epithelium of the alimentary canal modifies the absorbed liquid is now practically beyond question. In the first place there is a certain selection of the absorbed liquid from the general mixture of digested foodstuffs, and in the second place these absorbed substances are modified on their passages through the cells. We have to deal here with a clear case of secretion.

These examples of secretion in its broadest sense fall naturally into two groups: In the case of the gastric juice the elaborated fluid is selected or formed, to be poured out upon the surface of the mucous membrane for a particular use there. In the case of the lymph plasma there is a selection of the substances which are to filter or diffuse through the endothelium from one cavity or vessel into another cavity or vessel, to be retained in the system. In the case of absorption the selected and modified products of digestion are passed into the circulation, to be retained and further utilized. We thus have in the gastric juice an example of what has been called an *external secretion*, but in the formation of lymph and the modification of the products of absorption examples of an *internal secretion.*

The hypoblastic epithelium of the liver forms products which not only afford examples of the two kinds of secretion already named, but of a third kind which may be called simple *katabolites.* The *bile,* composed of substances which assist in digestion and in absorption, is an *external secretion;* the *glycogen* formed from the absorbed dextrose, and later thrown into the blood as dextrose, is an *internal secretion;* while the *urea* and related bodies formed in the liver are thrown into the blood, not to be utilized by the system, but to be *excreted* by the kidneys.

3. GLANDS.

In the above presentation of the subject the terms glandular epithelium and secretion have been used in the most general sense. The part which the epithelium plays in the elaboration of the products of digestion is still a subject of controversy. It will be best here to present more in detail the subject of external secretion and the specialized glandular epithelium (*glands*) which elaborate these secretions. Howell defines a gland as "a structure composed of one or more gland cells, epithelial in character, which forms a product—secretion—which is discharged either upon a free epithelial surface (external secretion), such as the skin or mucous membrane, or upon the closed endothelial surface (internal secretion) of the blood and lymph cavities."

The one example of a unicellular gland is the mucus-secreting goblet cell. It is more in harmony with the above presentation

FIG. 161

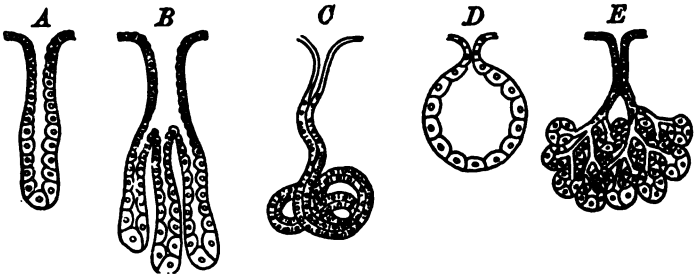
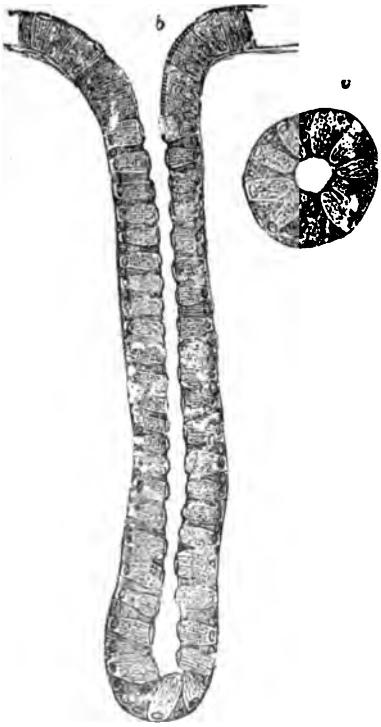


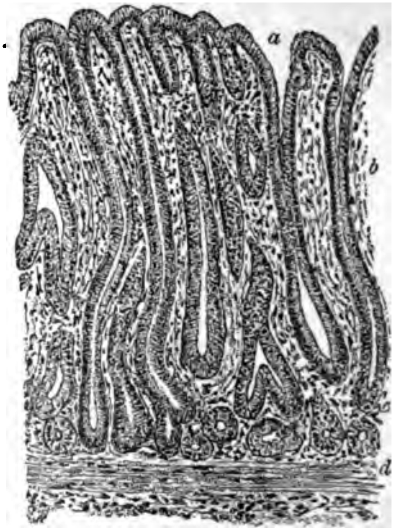
Diagram illustrating the types of glands: *A*, simple tubular; *B*, compound tubular; *C*, modified (coiled) tubular; *D*, simple saccular; *E*, compound saccular or racemose. (Piersol.)

FIG. 162



Simple tubular gland of large intestine: *b*, longitudinal section; *c*, cross-section

FIG. 163



Pyloric mucous membrane, showing compound tubular glands: *a*, mouth; *b*, duct; *c*, compound fundus, showing branches cut at various angles; *d*, musc. mucosæ. (After Benda.)

of the general physiology of glandular tissues to consider the goblet cells as representing unspecialized glandular tissue cells.

One phase of the process of differentiation which marks the progress of evolution is the development of *glandular organs.* A *glandular organ* or *gland* may be defined as a structure whose parenchyma is composed of a *specialized* portion of *glandular tissue*, which *elaborates* by *selection* or *formation* a *special secretion,* which is discharged either upon an epithelial surface (*external secretion*), or upon an endothelial surface (*internal secretion*).

Fig. 161 illustrates gland types. As examples of the simple tubular gland one may cite the glands of the large intestine (Fig. 162), the crypts of Lieberkühn, the peptic glands, etc.

The compound tubular gland is represented in human anatomy by the pyloric glands (Fig. 163) and the glands of Brunner as less complex examples; while the pancreas (Fig. 164), kidney, and liver represent compound tubular glands of successively increasing complexity. The sweat glands are coiled tubular glands. The simple saccular glands, though prominent in the amphibia as the mucus-secreting glands of the skin, do not occur in the higher animals. The compound saccular or racemose glands are represented in the human anatomy by the salivary glands (Fig. 165). Some authors classify these as compound tubular glands.

A discussion of the blood and nerve supply of the various digestive glands, of the histologic changes of the glandular epithelium during activity, and of the chemical composition of the secretion, will be found in connection with the physiology of the gland.

4. INTERNAL SECRETIONS.

a. Internal Secretion of the Ductless Glands.

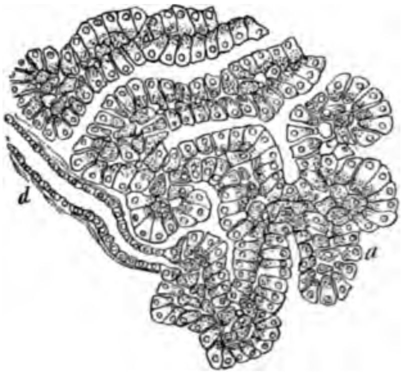
The functions of the vascular glands have been, until quite recently, a matter of somewhat vague speculation. Even now these functions are not by any means clearly established and fully understood; but so much work has been done, experimental and clinical, especially on the thyroid glands, the adrenal capsules, and the pituitary body, that the theories advanced as to their functions may be accepted as practically demonstrated.

1. **The Thyroid Glands and the Parathyroids.**—The thyroid gland is situated at the upper part of the trachea, and consists of two lateral lobes placed one on each side of that tube, and connected by a narrow transverse portion, the isthmus. The thyroid is of a brownish-red color. Its weight varies from one to two ounces. It is larger in females than in males, and becomes slightly increased in size during

menstruation and after maternity. It occasionally becomes enormously hypertrophied, constituting the disease called bronchocele, or *goitre.*

The accessory thyroids, or *parathyroids,* seem to occur in all mammals. One of these bodies is attached to the external or posterior surface of the lateral lobes of the thyroid; in some animals (dog, cat, rabbit, etc.) there is an additional lobe on each side, embedded in the substance of the thyroid proper. Histologically the parathyroids do not resemble the thyroid gland. They present the general appearance of embryologic tissue, and, for this reason, have been regarded as an immature form of thyroid tissue, which, under the stimulus of increased functional activity, is capable of developing into normal thyroid tissue.

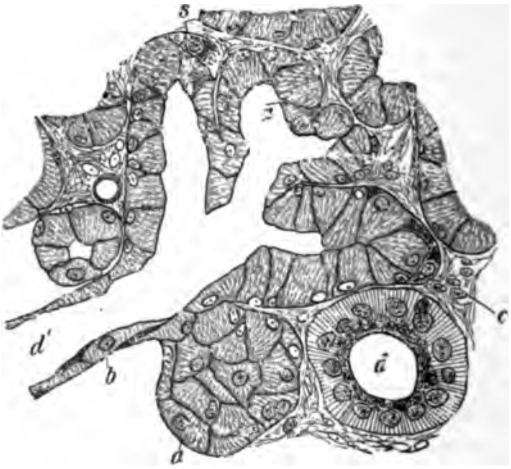
FIG. 164



Section of the pancreas of the dog: *d*, termination of a duct in the tubular alveoli, *alv.* (Klein.)

There is, however, no satisfactory evidence that such a transformation may take place. The histologic and embryonic evidence seems to indicate that the two tissues are not only fundamentally different in structure, but probably also different in origin.

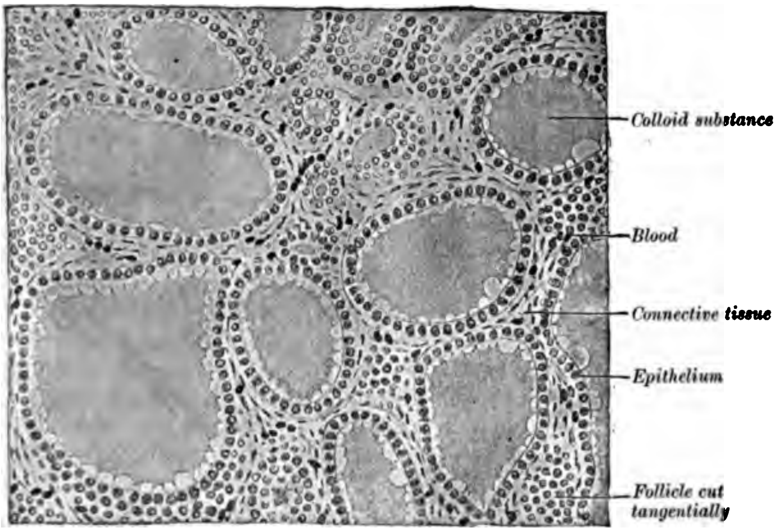
FIG. 165



Section of human submaxillary gland.

The thyroid body is invested by a thin capsule of connective tissue, hich projects into its substance and imperfectly divides it into asses of irregular form and size. When the organ is cut into it is en to be made up of a number of closed vesicles containing a yellow, airy fluid, and separated from each other by intermediate connective ssue. Each vesicle is lined by a single layer of epithelium, the cells f which, though differing somewhat in shape in different animals, ave always a tendency to assume the columnar form. Between the ithelial cells exists a delicate reticulum. The vesicles are of various zes and shapes, and contain as a normal product a viscid, homo-eneous, semifluid, slightly yellowish material, which frequently

FIG. 166



Section of human thyroid gland. (Szymonowicz.)

ontains blood, the red blood corpuscles of which are found in it in arious stages of disintegration and decolorization, the yellow tinge eing probably due to the hæmoglobin, which is thus set free from he colored corpuscles.

The thyroid gland is for the animal economy a most important, ndeed, necessary, organ. Its removal or destruction is followed y serious disturbances of nutrition, and is immediately or ultimately atal, because products of the normal metabolism attack and harm he central nervous system, so that nervous disturbances and depres-ion occur as well as disturbances of nutrition (tetanus and cachexia). he reintroduction of thyroid material (by grafting, by subcutaneous r intravascular injection, or by absorption from the alimentary canal) causes an amelioration or even an entire removal of all toxic symptoms.

It follows from the foregoing that the thyroid tissue produces normally some material which is in some way essential to the nutrition of the body, and which acts as an antitoxic to those products of normal metabolism which produce tetanus and cachexia in thyroidectomized animals. Such a material has been isolated by Baumann, and is called thyroiodin, or iodothyrin. It is an organic compound of iodine, is produced by the thyroid gland from traces of iodine contained in the food and carried into the blood. According to the experiments of Roos, it preserves the beneficial effects of thyroid tissue, and acts like the latter in thyroidectomized animals.

The fact that extracts of thyroid tissue, or iodothyrin, when absorbed into the blood, ameliorate or remove the evil effects resulting from a loss of function of the thyroid gland seems to prove that the normal function of the thyroid is to give off a material to the blood which in some way affects favorably the nutrition of all or a part of the tissues of the body. Histologic research shows that, as far as the thyroid bodies proper are concerned, this secretion is contained in the so-called colloidal material which accumulates in the interior of the vesicles, and that the mechanism of secretion is a rupture of the walls of the vesicles at some point, whereby the contents are discharged into the surrounding lymph spaces.

The most important fact to be discovered is the manner of action of this secretion upon the tissues of the body. The most tenable theory is that the secretion of the thyroid acts normally by promoting or regulating the metabolism of other parts of the body, particularly perhaps the nervous system. Here are two facts of great importance to be remembered in this connection: (I) that complete removal of thyroid tissue causes malnutrition, affecting, it seems, especially the nervous system, and (II) that the injection or ingestion of thyroid extracts in this condition restores metabolism more or less completely to a normal state.

An interesting phase in the physiology of the thyroid is the functional relation between the thyroid and the parathyroid bodies. This relation has been problematic and has occasioned considerable controversy and a vast amount of experimentation. The most recent and reliable results are those of Mousu from a study of over 150 thyroidectomies and parathyroidectomies. Moussu arrives at these conclusions:

(I) "The organs of the thyroid system have two distinct functions, one thyroidal and one parathyroidal. The thyroids do not act vicariously for the parathyroids, and *vice versa*.

(II) "*The thyroid function is the same for all domestic animals* and for birds. Its suppression has always the same result—viz., *development of cretinism*, if it is caused under identical conditions.

(III) "*Cretinism occurs only in the young.* It is the more acute the earlier the subjects are operated on.

(IV) "*In adults thyroidectomy does not cause acute symptoms,* not even in carnivora. The operation is generally survived for a long period, but may be followed by progressive cachexia or by myxœdema.

(V) "The *parathyroid function is for the most vital conditions of life indispensable.* It seems to influence immediately the nutrition of tissues.

(VI) "*Its suppression causes rapid death if total,* alarming disturbances if partial.

(VII) "*The acute symptoms,* such as tetanus, rapid pulse, dyspnœa or polypnœa, etc., following operations on the goitre in man *are parathyroid symptoms.*

(VIII) "*The chronic symptoms,* such as lowering of temperature, weakening of the intellectual faculties, myxœdema, etc., *are exclusively thyroid symptoms.*

(IX) "Strumipriva cachexia must develop fatally if thyroïdectomy is performed during infancy and adolescence.

"In all operations on the thyroid organs the first duty of the surgeon is to look for and *to respect the parathyroids in all cases.*"

Von Cyon has made a full and exhaustive study of the relation of the thyroid gland and the heart. He states that a suppression of the thyroid function (through illness or extirpation) and likewise an increase of the functional activity (injection of iodothyrin) have a very great influence on the entire nervous system of heart and bloodvessels. He proves that the vagus participates in the innervation of the thyroid gland, or is, at least, closely connected with it, and offers, in his discussion of the hypotheses on the functions of the thyroid the following conclusions:

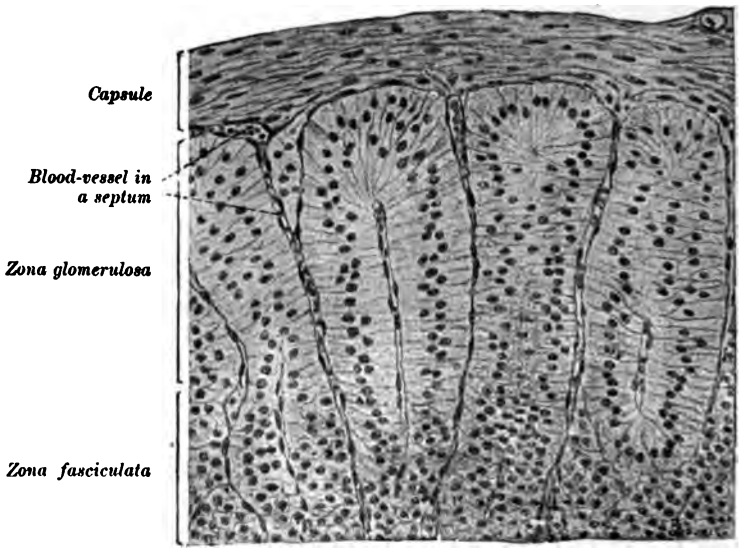
(X) "The function of the thyroid gland is to make harmless the salts of iodine, which have a toxic effect on the vagi and sympathetic nerves, by converting them into an organic compound, the *iodothyrin,* which has a stimulating effect on the same nerves, and increases their power.

(XI) "The thyroid gland functions mechanically as a *safeguard for the brain against engorgement.* In a sudden increase of blood pressure, whether from increased activity of the heart or from increased resistance of the peripheral blood currents, the thyroid gland is capable of passing a large amount of blood in a short time through its vessels, taking it thus directly from the arterial back into the venous circulation and preventing its entrance into the cerebral circulation."

Clinically but few attempts have been made to separate thyroid and parathyroid function. Pineles[1] observed that thyreoaplasia is never associated with tetany when normal parathyroids are present, while after thyroidectomy, where the parathyroids are also removed, tetany frequently results. He also noted that most cases of postoperative tetany follow bilateral partial thyroidectomy (in such an operation all the parathyroids are removed). He thus suggests the probable relationship of tetania strumipriva, tetany after parathyroidectomy, idiopathic cases of tetany, and parathyroid insufficiency.

Benjamins,[2] in Van Iterson's clinic, studied the relationship between postoperative symptoms in thyroidectomy and the parathyroids. Of the 8 cases studied, in 4 instances no glands were found in the removed mass, yet no ill effects resulted; in 1 case one gland was found, and in twenty-four hours after operation the patient developed tetany which subsided in eight days. In 2 cases three glands were found and tetany occurred three to five days after operation and lasted only one week. In 1 case he found one gland and no ill effects resulted. He thus concludes that no relationship between postoperative tetany and parathyroid insufficiency can be established.

FIG. 167



From the cortical substance of the adrenal of a dog. (Szymonowicz.)

Vessali and Generali,[3] observed that tetany can follow when parathyroids are removed with the thyroid, and that cachexia strumipriva and myxœdema result, without tetany, when the parathyroids are saved.

Moussu[4] treated an exophthalmic goitre case with good results by parathyroid feeding, but the case soon died from an existing tuberculosis. MacCallum[5] searched for the parathyroids in 8 cases of exophthalmic goitre operated upon. He found parathyroid tissue in only 4 of them. In all cases where the parathyroids were found they were smaller than normal and in 2 instances showed parenchymatous degeneration. In a very acute case of exophthalmic goitre which came to autopsy he was unable to find any parathyroid tissue. A case of exophthalmic goitre treated with parathyroids showed no improvement. He also suggests the relationship of epilepsy and parathyroid insufficiency, because he observed epileptiform convulsions in parathyroidectomized dogs.

Jeandelize[6] thinks there exists a relationship between parathyroid insufficiency and puerperal eclampsia.

In summarizing the meagre clinical evidences at hand it may be said that parathyroid insufficiency seems to be associated with the muscular hypertonicity, manifesting itself as a tremor in exophthalmic goitre and as tetany after parathyroidectomy.

2. **The Suprarenal Capsules.**—The suprarenal capsules, or bodies, are found constantly in all classes of vertebrates, and seem, therefore, to be organs of fundamental importance. They are two small, flattened, glandular bodies, of a yellowish color, situated at the back part of the abdomen, behind the peritoneum, and immediately in front of the upper part of either kidney.

On making a perpendicular section the glands are seen to consist of two substances—external or cortical, and internal or medullary. The former, which constitutes the chief part of the organ, is of a deep-yellow color and consists chiefly of narrow columnar masses placed perpendicularly to the surface. The medullary substance is soft, pulpy, and of a dark-brown or black color.

Brown-Séquard stated in 1856 that extirpation of both suprarenals is usually fatal to the animal, and more rapidly fatal than the removal of both kidneys. Recent experiments seem to corroborate this statement. The fact that in some species of animals accessory suprarenals occur may explain why extirpation is not always fatal.

On removal of only one of the bodies no noticeable disturbances have been observed. After complete removal, with ultimately fatal results, the prominent symptoms were: Extreme muscular weakness, asthenia, and, in the case of dogs examined during this period, a great fall in the blood pressure, together with a feeble heart beat, have been ascertained. It is worthy of notice that in Addison's disease these symptoms occur, together with the familiar pigmentation; the explanation of these symptoms is, however, still *sub judice*.

The effects of injections of suprarenal extracts in living animals, on the vascular and respiratory organs, have recently been studied by Oliver and Schaefer, and by Cybulski and Szymonowicz.

Extracts of the medullary portion of the suprarenals, injected into the veins of an animal, caused pronounced slowing of the heart beat and a large rise of blood pressure. If the animal was first given atropin to paralyze the inhibitory nerves to the heart, or, if the vagi were previously cut, the injection was followed usually by a marked quickening instead of slowing of the heart beat, and by a greater rise of blood pressure. The organs of respiration were not affected so seriously. A temporary slowing and shallowing of the respirations could usually be noticed. According to Oliver and Schafer the heart is influenced by the direct action of the extract upon the cardio-inhibitory centre. The enormous rise of blood pressure is due to constriction of the arterioles.

Blood drawn from the suprarenal vein and injected into the circulation of normal animals causes the same symptoms, though less intense, as injection of extract, while blood drawn from other veins has no effect.

From the above it seems certain that a material formed by the secretory activity of the gland cells occurs normally in the venous blood flowing from the gland. Probably it is a normal product of metabolism of the medullary cells of the gland, and is secreted and discharged directly into the blood. It must, therefore, exert continually a *stimulating effect upon the heart and bloodvessels. This assumption is confirmed by the fact that after complete extirpation of both glands the blood pressure is greatly depressed.*

The normal function of the suprarenal bodies consists in furnishing this stimulating substance to the blood. It is believed that its effects are exerted mainly on the muscular tissue; at any rate, it has a general tonic or augmenting action on all varieties of muscles found in the body, or perhaps the effect may be on the nerve centres controlling the muscular action rather than on the tissues directly. It is impossible at present to decide the exact mode of action.

3. **Hypophysis Cerebri.**—The hypophysis cerebri (or pituitary body) is a small reddish-gray mass, weighing from five to ten grains. It is very vascular and consists of two lobes, separated from one another by a fibrous lamina. Of these, the anterior is the larger, of an oblong form and somewhat concave behind, where it receives the posterior lobe, which is round. The two lobes differ both in origin and structure. The anterior lobe, of a dark, yellowish-gray color, is developed from the ectoderm of the buccal cavity, and resembles to a considerable extent, in microscopic structure, the thyroid body. It is thus a glandular structure. According to Haller it cannot be called strictly a ductless gland, since it possesses an imperfectly developed system of ducts opening between the dura and pia mater. It is evidently a secretory structure, and the fact that the secretion is discharged between the meningeal membranes suggests some special connection with the physiology of the brain. The posterior lobe is developed by an outgrowth from the embryonic brain, and during fetal life contains a cavity which communicates through the infundibulum with the cavity of the third ventri-

le. It is always small and has the appearance of a rudimentary rgan.

The clinical observations as to the function of the pituitary body have been limited to the glandular lobe. In many cases of acromegalia this presents pathologic changes.

Howell has made experiments with extracts of both lobes of the hypophyses (of sheep) separately. Injections of extracts of the glandular lobe gave little or no effect, while *injections of extracts of the infundibular lobe had a distinct and remarkable effect on the heart rate and blood pressure, which resembles in some respects, and differs in others from that of suprarenal extracts.*

Extracts injected in normal animals with vagi intact caused a pronounced slowing of the heart beat, similar to that from suprarenal extracts, but lasting a much longer time. The heart beats were not only slowed, but considerably augmented in force. The blood pressure rises to a considerable extent, owing apparently to the peripheral constriction of bloodvessels. If the dose was a maximal one, and followed too quickly by a second injection, there was little or no effect, but if the dose was not too strong, and sufficient time was allowed for the effects to wear off, they could be repeated. With each repetition the effects decrease progressively in intensity.

b. Internal Secretion of Liver, Pancreas, Testis, etc.

Because the liver and pancreas possess ducts through which they pour copious secretions into the alimentary canal it was, for a long time, assumed that the elaboration of their respective external secretions was their sole function.

It has now, however, been demonstrated that not the least important work of the glands in question is the formation of substances which, thrown into the blood or lymph, profoundly influence the course of metabolism. Only a brief mention of these activities of the glands in question need be made here.

1. **The Liver.**—The bile is the external secretion of the liver. Its internal secretions are, however, of vastly greater importance. Chief among the internal secretions is *glycogen.* Important products of liver activity are: *urea, uric acid,* and the *purin bodies.* The relation of these substances to metabolism is discussed in detail in the chapters on Metabolism and Excretion.

2. **The Pancreas.**—The experiments of von Mering (*Arch. f. exp. Path. u. Pharm.*, 1890, vol. xxvi. p. 371) and the reports of Minkowski (*Ibid.*, vol. xxxi. p. 85) introduce the pancreas in a new role. Its extirpation results in the excretion of sugar in the urine (glycosuria), even when there is no sugar or starch in the food. From this it is evident: (I) that sugar may be formed from nitrogenous food materials, and (II) that the pancreas controls the final katabolism

of sugar in the tissues, whether it exerts this influence through the secretion of a special enzyme or through some substance which exerts an inhibitory effect upon sugar formation in the liver and muscles.

Opie was the first to demonstrate a definite etiologic relationship between glycosuria and the islands of Langerhans in the pancreas. By careful histologic methods he demonstrated the predominance of these islands in the tail portion of the organ, thus clearing the mystery as to why a glycosuria does not ensue in so many cases of complete destruction of the head.

In considerably more than half of the cases of diabetes Opie found pancreatic disease in the form of sclerosis and hyaline degeneration involving these interacinar cellular areas of Langerhans.

In operation on the pancreas it is only necessary to leave a portion of the gland, particularly the tail (one-fourth to one-fifth), to prevent the appearance of sugar in the urine.

3. The Testis and Ovary.—The removal of these glands early in the life of an animal exerts a profound influence upon the physical development. The male, after loss of the testes, develops into a being possessed of male and female physical and psychical characteristics about equally balanced; while the female, after loss of the ovaries, develops similarly into a neutral adult lacking those characteristics which we recognize as distinctive of the female.

The work of Brown-Séquard (*Arch. de physiol. norm. et path.*, 1889 *et seq.*) demonstrates that the animal receives from these glands an internal secretion which acts principally on and through the central nervous system and leads to the development of those characteristics which are distinctly male or female, as the case may be. The sum of these characteristics in the male may be designated by the term *virility*. There is no corresponding term by which we may designate the sum of female characteristics.

The glands begin their activity at the beginning of the adolescent period and continue their influence until the beginning of the senile period in the male and the climacteric in the female.

The active substance in the testicular secretion seems, from the experiments of Poehl, to be *spermin* ($C_5H_{19}H_2$). This substance appears in the external secretion of the testes. When injected it exerts an extraordinary influence as a tonic to the neuromuscular system.

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D. CHEMICAL INTRODUCTION.

1. FUNDAMENTAL CARBON COMPOUNDS.

One cannot gain a definite idea of the metabolic processes of nutrition without knowing the chemical composition of the body and of foodstuffs, and following, as closely as may be, the chemical reactions which take place during the processes of digestion, and the processes of constructive and of destructive metabolism.

The author proposes to summarize here a few of the facts of chemistry that may be convenient for reference during the study of the succeeding chapters on nutrition.

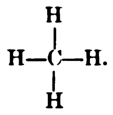
The chemistry of the carbon compounds is the basis for physiologic chemistry.

The compounds of carbon with hydrogen form the basis for the consideration of all of the higher carbon compounds.

The simplest compound of carbon and hydrogen is marsh gas, or *methane*, CH_4.

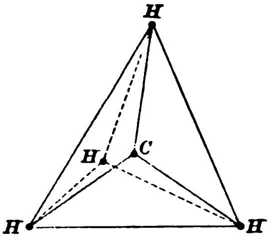
A clear notion of the relations of various compounds involved in nutrition can only be gained through a study of the structural formulæ of those compounds. Let us, therefore, use the structural formulæ as far as possible.

The structural formula of methane is:



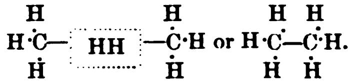
$$\begin{array}{c} H \\ | \\ H\text{—}C\text{—}H. \\ | \\ H \end{array}$$

FIG. 168



Space relations of the atoms in methane.

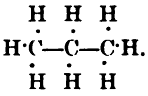
As these five atoms must be conceived as occupying positions in tridimensional space, we may assume that they are symmetrically arranged with the carbon atom in the centre. That gives us a tetrahedron with each hydrogen atom equidistant from each other hydrogen atom. The space relations of the atoms being as yet largely conjectural, we will be content with representing the molecule on a plane surface. All of the hydrogen atoms are displaceable. They may be displaced singly by monads or monivalent radicals, or by two diads, etc. One fundamental method of combination of carbon atoms is through dropping two hydrogen atoms:



$$\begin{array}{ccccc} H & & H & & H\ \ H \\ H\cdot C- & \boxed{HH} & -C\cdot H & \text{or} & H\cdot C-C\cdot H. \\ H & & H & & H\ \ H \end{array}$$

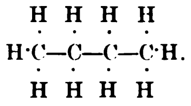
This compound is called *Ethane*, and may be written C_2H_6 or $CH_3—CH_3$.

The third carbon compound in the series is *Propane*, written C_3H_8; $CH_3—CH_2—CH_3$ or:



$$\begin{array}{c} H\ \ H\ \ H \\ H\cdot C-C-C\cdot H. \\ H\ \ H\ \ H \end{array}$$

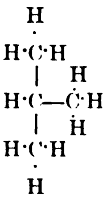
The fourth member of the series is *Butane:* C_4H_{10}; $CH_3—CH_2—CH_2—CH_3$ or:



$$\begin{array}{c} H\ \ H\ \ H\ \ H \\ H\cdot C-C-C-C\cdot H. \\ H\ \ H\ \ H\ \ H \end{array}$$

The series may be continued through *Pentane, Hexane, Heptane, Octane, Dodecane,* and *Hecdecane,* which are called the normal paraffins.

If one study the structural formula of butane, he finds that the same number of atoms may be differently arranged and still satisfy all of the bonds:



$$\begin{array}{l} \ \ \ \ H \\ H\cdot C\cdot H \\ \ \ \ \ |\ \ \ H \\ H\cdot C-C\cdot H \\ \ \ \ \ |\ \ \ H \\ H\cdot C\cdot H \\ \ \ \ \ H \end{array}$$

The two forms of butane which exist can only be accounted for in this way. This property of the molecule is called *Isomerism*. The first butane is *normal butane*, the second *isobutane*. As the series advances the possibility of isomerism rapidly increases.

Let us now turn our attention to some of the derivatives of the series of hydrocarbons. If one of the atoms of hydrogen be removed from CH_4 a monad radical methyl will result: *Methyl* = CH_3.

In a similar way arise the *monad radicals:*

Ethyl = C_2H_5 —; $CH_3 — CH_2$ —.
Propyl = C_3H_7 —; $CH_3 — CH_2 — CH_2$ —.
Butyl = C_4H_9 —; *Pentyl* = C_5H_{11} —; *Hexyl* = C_6H_{13} —, etc.

When one of the monad radicals takes the place of one of the hydrogen atoms of a molecule of water an alcohol results:

$H{\cdot}O{\cdot}CH_3$, methyl alcohol.

Another way of representing the matter is to conceive one of the atoms of hydrogen of the hydrocarbon (methane, ethane, etc.) to be exchanged for OH, or *hydroxyl*, which may be written: CH_3OH.

In the same way arises the series of *primary monatomic alcohols:*

Ethyl alcohol, C_2H_5OH; or $CH_3 — CH_2OH$.
Propyl alcohol, $C_3H_7{\cdot}OH$; or $CH_3 — CH_2 — CH_2OH$.

In the propyl alcohol it is evident that the hydroxyl may displace a hydrogen from the central carbon atom instead of one of the end atoms, giving the formula $CH_3—CHOH—CH_3$, or secondary propyl alcohol, which is the first one of a series of *secondary monatomic alcohols.*

Table showing the normal paraffin series with the corresponding radicals and primary monatomic alcohols:

THE PARAFFINS.	RADICALS.	ALCOHOL.
General formulæ C_nH_{2n+2} *or* $CH_3(CH_2)_{n-2}CH_3$	C_nH_{2n+1} *or* $CH_3—(CH_2)_{n-2}CH_2OH—$	$C_nH_{2n+1}.OH$ *or* $CH_3(CH_2)_{n-2}CH_2OH$
Methane, $CH_3—H$	Methyl, $CH_3—$	Methyl alcohol, $H.CH_2OH$
Ethane, $CH_3—CH_3$	Ethyl, $CH_3—CH_2—$	Ethyl alcohol, $CH_3—CH_2OH$
Propane, $CH_3—CH_2—CH_3$	Propyl, $CH_3—CH_2—CH_2—$	Propyl alcohol, $CH_3—CH_2—CH_2OH$
Butane, $CH_3(CH_2)_2CH_3$	Butyl, $CH_3—(CH_2)_2—CH_2—$	Butyl alcohol, $CH_3—(CH_2)_2—CH_2OH$
Pentane, $CH_3—(CH_2)_3—CH_3$	Pentyl, $CH_3—(CH_2)_3—CH_2—$	Pentyl alcohol, $CH_3—(CH_2)_3—CH_2OH$
Hexane, $CH_3—(CH_2)_4—CH_3$	Hexyl, $CH_3—(CH_2)_4—CH_2—$	Hexyl alcohol, $CH_3—(CH_2)_4—CH_2OH$
Heptane, $CH_3—(CH_2)_5—CH_3$	Heptyl, $CH_3—(CH_2)_5—CH_2—$	Heptyl alcohol, $CH_3—(CH_2)_5—CH_2OH$
Octane, $CH_3—(CH_2)_6—CH_3$	Octyl, $CH_3—(CH_2)_6—CH_2—$	Octyl alcohol, $CH_3—(CH_2)_6—CH_2OH$

Any primary alcohol when oxidized step by step undergoes the following change as the first step:

$$\underset{\text{Ethyl alcohol.}}{CH_3—CH_2{\cdot}OH} + \underset{\text{Oxygen.}}{O} = \underset{\text{Water.}}{H_2O} + \underset{\text{Ethyl aldehyde.}}{CH_3—CHO.}$$

The second step consists in the addition of an oxygen atom to the molecule thus: ethyl aldehyde + oxygen = acetic acid (number 2 in the fatty acid series).

$$CH_3—CHO + O = CH_3—COOH.$$

The group COOH is called the *carboxyl* group.

The following table shows the *primary monatomic alcohols* and the corresponding oxidation products—aldehydes and fatty acids:

ALCOHOLS.	ALDEHYDES.	FATTY ACIDS.
$CH_3-(CH_2)_{n-2}CH_2.CH$	$CH_3-(CH_2)_{n-2}CHO$	$CH_3.(CH_2)_{n-2}COOH$
Methyl alcohol, $H.CH_2.OH$	Methyl aldehyde, $H.CHO$	Formic acid, $H.COOH$
Ethyl alcohol, $CH_3—CH_2.OH$	Ethyl aldehyde, $CH_3—CHO$	Acetic acid, $CH_3—COOH$
Propyl alcohol, $CH_3—(CH_2)_1—CH_2.OH$	Propyl aldehyde, $CH_3—(CH_2)_1—CHO$	Propionic acid, $CH_3—(CH_2)_1—COOH$
Butyl alcohol, $CH_3—(CH_2)_2—CH_2.OH$	Butyl aldehyde, $CH_3—(CH_2)_2—CHO$	Butyric acid,[1] $CH_3—(CH_2)_2—COOH$
Pentyl alcohol, $CH_3—(CH_2)_3—CH_2.OH$	Pentyl aldehyde, $CH_3—(CH_2)_3—CHO$	Valeric acid,[1] $CH_3—(CH_2)_3—COOH$
		Caproic acid, $CH_3—(CH_2)_4—COOH$
		Œnanthylic acid, $CH_3—(CH_2)_5—COOH$
		Octylic acid, $CH_3—(CH_2)_6—COOH$
		Caprylic acid, $CH_3—(CH_2)_7—COOH$

Higher normal fatty acids whose formulæ may be written from the above generalized formula are: 10th Capric acid, 12th Lauric acid, 14th Myristic acid, 16th Palmitic, 17th Margaric, 18th Stearic, 20th Arachnic, 30th Melissic acid.

The oxidation of the primary monatomic alcohols gives rise to a series of *aldehydes* of the *monatomic alcohols*.

The oxidation of the secondary monatomic alcohols gives rise to a series of *ketones*. The first step in the oxidation may be represented thus:

$$CH_3—CHOH—CH_3 + O = H_2O + CH_3—CO—CH_3.$$

Secondary propyl alcohol + O = H_2O + ketone of secondary propyl alcohol.

Note that the ketone contains two methyl radicals joined by CO. Its chemical name is Dimethylketone. The ketone derived from secondary butyl alcohol has the formula: $CH_3—CH_2—CO—CH_3$, and may be called Methylethylketone. A further oxidation breaks up the ketone into its elements, yielding acids which contain fewer atoms of carbon than the secondary alcohol from which they were derived.

The Diatomic Alcohols, or Glycols.—The combination of two carbon atoms in the paraffin-ethane ($CH_3—CH_3$) may, under certain conditions, be brought about with fewer than six hydrogens, yet all of the bonds of carbon will be satisfied. The following formula shows the structure of this molecule:

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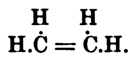
[1] Corresponding to butyric acid is isobutyric acid, written: $(CH_3)_2—CH—COOH$; and corresponding to valeric acid is its isomere, isovaleric acid, or the common valerianic acid $(CH_3)_2—CH—CH_2—COOH$.



$$\mathrm{H.\overset{H}{\dot{C}}=\overset{H}{\dot{C}}.H.}$$

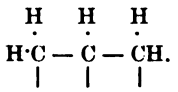
It is called Ethylene and has the general formula CnH$_2$n.

It is also called olefiant gas, and is the first of a series of olefines.

Derived from the olefines are the glycols, or diatomic alcohols, oxidation of which gives rise to the *Lactic acid series* (monobasic), or the *Oxalic acid series* (dibasic).

Lactic acid has the formula: CH$_3$—CHOH—COOH; Oxalic acid, COOH—COOH.

The Triatomic Alcohols and Derivatives.—The series of triatomic alcohols begins with the tricarbon radical *propenyl*, which is derived from propane:



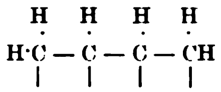
$$\mathrm{H{\cdot}\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}H.}$$

When the three bonds are satisfied with hydroxyl we have propenyl alcohol, *glycerol* or *glycerin:* CH$_2$OH—CHOH—CH$_2$OH.

It is evident that in the propenyl radical two of the open bonds may be reciprocally satisfied, giving rise to a monad radical allyl and its corresponding alcohol: CH$_2$=CH—CH$_2$OH.

The acid series corresponding to this alcohol is called Oleic Acid Series, oleic acid being the XVIII. member of the series CH$_3$—(CH$_2$)$_{14}$—(CH)$_2$—COOH.

The tetratomic alcohols begin with the derivative of butane, having the formula:

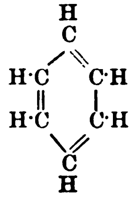


$$\mathrm{H{\cdot}\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}-\overset{H}{\underset{|}{C}}H}$$

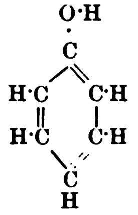
When each of these open bonds is satisfied we have the tetrad alcohol *erythrol:* CH$_2$OH—(CHOH)$_2$—CH$_2$OH. *The hexatomic alcohols* begin with mannitol or mannite, whose formula is CH$_2$OH—(CHOH)$_4$—CH$_2$OH. (See Carbohydrates, p. 303.)

The Benzole Derivatives.

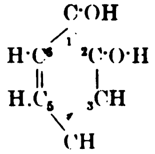
The carbon compounds thus far considered are arranged with the carbon atoms, forming a chain. There is some departure from this rule in the isomeres of the fundamental compounds, but the "chain type" is dominant. In benzine and the benzole derivatives we have a radical departure from this type in the "ring type."



Note that the four bonds of the carbon atoms are reciprocally satisfied as indicated, the particular location of the double bond being, of course, conventional. Note also that this hydrocarbon has a much larger proportion of carbon than is the case in the chain-type of hydrocarbons. The hydrogen atoms are displaceable by monads or monad radicals, thus giving rise to a long series of *Benzole derivatives* or "Aromatic compounds." Phenol, Carbolic acid, Phenylhydroxide, or hydroxybenzole has the following formula:



If two of the hydrogen atoms be displaced by hydroxyl the relative position of these two hydroxyls is not a matter of indifference; if they are adjacent to each other, thus:



it is called *ortho*-dihydroxybenzole (*catechol*).

If the two hydroxyls are not adjacent, but occupy the positions 1.3 or 1.5 the compound is called *meta*-dihydroxybenzole (*resorcinol*). If the radicals are symmetrically opposite, as at position 1.4, the compound is a *para*-compound, in this case *para*-dihydroxybenzole (*quinol* or *hydroquinone*).

A few examples will show the general structure of the bodies.

(1) Orthohydroxybenzoic, or *salicylic acid:*

$$C_6H_4{\cdot}OH - COOH.$$

(2) Paraethylphenol or para-hydroxyphenyl ethyl:

$$C_6H_4{\cdot}OH -- C_2H_5.$$

Parahydroxyphenyl-*a*-amidopropionic acid, or *Tyrosin:*

$$C_6H_9OH - CH_2 - CHNH_2 - COOH.$$

2. THE CARBOHYDRATES.

a. Glycoses, or Monosaccharides.

This most important class of organic compounds includes various aldehydes and ketones of the higher alcohols, beginning with the triatomic propenyl alcohol, glycerol.

The following reaction indicates the course which similar changes take in the higher alcohols as well as in glycerols:

$$2(CH_2OH - CHOH - CH_2OH) + O_2 = 2H_2O + \left\{\begin{array}{l} CH_2OH - CHOH - CHO. \\ CH_2OH - CO - CH_2OH. \end{array}\right.$$

$$\text{2 Glycerol + Oxygen = Water + 2 Glycerose; } i.e., \left\{\begin{array}{l} \text{Aldehyde of Glycerol.} \\ \text{Ketone of Glycerol.} \end{array}\right.$$

The aldehydes in the carbohydrate series are called *aldoses,* while the ketones are called *ketoses.* The oxidation of glycerol results, as above indicated, in a mixture of equal parts of the aldose and ketose of glycerol.

The *monosaccharides* are classified according to the number of carbon atoms in the chain. Those with three carbons are called *Trioses,* those with four carbons *Tetroses,* those with five carbons *Pentoses,* and those with six carbons *Hexoses.* The monosaccharides may be classified as follows:

(*a*) **Trioses**—Ex. Glycerose, a mixed aldose and ketose ($C_3H_6O_3$).

(*b*) **Tetrose**—Ex. Erythrose, the aldose of eruthrol ($C_4H_8O_4$).

(*c*) **Pentose**—Ex. Xylose and Arabinose, both having the formula ($C_5H_{10}O_5$).

(*d*) **Hexoses** or **Glucoses** represent aldoses and ketoses of the hexamotic alcohols, mannitol, dulcitol, and sorbitol.

(*α*) DEXTROSE, d-glucose, grape-sugar, is the aldose of sorbitol: $CH_2OH - (CHOH)_4 - CHO$, or $C_6H_{12}O_6$. Dextrose is a sweet, crystalline substance, whose solutions rotate polarized light to the right—*i. e.,* dextrorotary.

(*β*) LEVULOSE, d-fructose, fruit-sugar, is the ketose of mannitol: $CH_2OH(CHOH)_3—CO—CH_2OH$. This sugar occurs in honey and in many fruits.

(*γ*) GALACTOSE, or d-galactose, is the aldose of dulcitol.

(*δ*) MANNOSE is the aldose of mannitol.

The hexoses or glucoses are incomparably more important than any of the other glycoses because they enter so largely into the dietary of man and the higher animals.

b. Sucroses, or Disaccharides.

These are double-grouped sugars which represent a combination of two hexose groups minus a molecule of water.

(*a*) **Saccharose**, or cane-sugar, is composed of a combination of dextrose and levulose as follows: The dextrose loses OH from a CHOH group and levulose loses H from a CHOH group, thus releasing a bond in each chain. These bonds hold the chains together into a disaccharide molecule. Dextrose + levulose — H_2O = *Saccharose* ($C_{12}H_{22}O_{11}$).

(*b*) **Lactose**, or milk-sugar, is likewise composed of a galactose group with a dextrose group dehydrated: Dextrose + galactose — H_2O = *Lactose* ($C_{12}H_{22}O_{11}$).

(*c*) **Maltose** is an end product of the action of amylolytic ferments upon starch, the hydrolysis of the starch molecule resulting in its cleavage into maltose and a dextrine. Dextrose + dextrose — H_2O = maltose. Its quantitative formula is $C_{12}H_{22}O_{11}$. In common with dextrose, lactose, and fructose it reduces Fehling's solution.

c. The Polysaccharides, or Amyloses.

To this class of carbohydrates belong the ***starches***, ***gums***, ***dextrins***, and *cellulose*. The molecular constitution is unknown. The members of the class have in common the general formula $(C_6H_{10}O_5)_n$. To the quantity *n* various values have been assigned.

d. Classification of Carbohydrates.

- Carbohydrates
  - Monosaccharides, or glycoses
    - Trioses: glycerose.
    - Tetroses: erythrose.
    - Pentoses: xylose, arabinose.
    - Hexoses, or glucoses
      - Dextrose, or grape-sugar.
      - Levulose, fructose, or fruit-sugur.
      - Galactose.
      - Mannose.
  - Disaccharides, or sucroses
    - Saccharose.
    - Lactose.
    - Maltose and isomaltose.
  - Polysaccharides, or amyloses
    - The dextrins
      - Amylodextrin.
      - Erythrodextrin.
      - Achroödextrin α.
      - Achroödextrin β.
    - The gums: gum arabic, etc.
    - The starches
      - Vegetable starch,
      - Animal starch; glycogen.
    - Cellulose.

3. THE FATS.

In our review of the fundamental carbon compounds we have found a series of normal fatty acids which are derived from the monatomic alcohols. These fatty acids have the general structural formula:

$CH_3—(CH_2)_{n-2}—COOH$. The sixteenth member of this series is palmitic acid, which has the formula $CH_3—(CH_2)_{14}—COOH$.

Propenyl alcohol, or glycerol, is the first member of the series of triatomic alcohols and has the formula: $CH_2OH—CHOH—CH_2OH$ or $C_3H_5(OH)_3$.

When these two bodies are brought together under proper conditions there is a combination of one molecule of glycerol with three molecules of the fatty acid to form one molecule of *Palmitin* or *Tripalmitin*, one of the common fats:

$$\left.\begin{array}{l} CH_3(CH_2)_{14}COO\,H + HO\,CH_2 \\ \qquad\qquad\qquad\qquad\qquad\quad\; | \\ CH_3(CH_2)_{14}COO\,H + HO\,CH \\ \qquad\qquad\qquad\qquad\qquad\quad\; | \\ CH_3(CH_2)_{14}COO\,H + HO\,CH_2 \end{array}\right\} = 3H_2O + [CH_3(CH_2)_{14}COO]_3C_3H_5.$$

3 Palmitic acid + Glycerol = Water + Palmitin or Tripalmitin.

In a similar way *Stearin* or *Tristearin* is formed from three molecules of stearic acid and glycerol, and has the formula: $[CH_3(CH_2)_{16}\text{-}COO]_3C_3H_5$.

Olein is a similar combination of three molecules of oleic acid (which is the eighteenth member of the oleic acid series, derived from the triatomic alcohols), and has the formula: $[CH_3(CH_2)_{14}(CH)_2\text{-}COO]_3C_3H_5$ or $(C_{18}H_{33}O_2)_3C_3H_5$. Palmitin, stearin, and olein are the fats which are deposited in the adipose tissue of the animal body. Palmitin has a melting point of 45° C.; stearin, 53° to 66° C.; olein, 0° C. The animal fats are mixtures of these three constituents in various proportions peculiar to each species of animal.

The melting point of a mixture is the proportional average for the fats which compose the mixture. Both palmitin and stearin have a melting point above animal temperature. The fat of the animal body is always in a fluid state during life. The mixture of the three constituents must include sufficient olein to ensure the fluidity of the fat at body temperature. But the melting point of the fat of different animals varies through a wider range than does the temperature of the animals.

4. THE PROTEINS.

The term protein is a general one which includes a class of compounds of which egg albumen, serum albumin, hæmoglobin, and fibrin may serve as examples. Though any of these may serve as animal food in common with the carbohydrates and the fats, they stand much nearer to living protoplasm than do carbohydrates and fats.

In fact the living matter which we call protoplasm and which possesses the marvelous power of liberating the energy which we call life, if deprived of life and subjected to chemic analysis, is shown to be only a mixture of proteins, together with various substances which may represent foodstuffs, in various stages of anabolism or cleavage products of protoplasm in various stages of katabolism. Just what changes take place between the departure of life and the resolution of the protoplasm into the various compounds just referred to, it is impossible to say. Of the various foodstuffs and katabolites found in protoplasm it is likely that all or nearly all are purely incidental to the life processes, and that the matter which actually possesses life—*i. e.*, the true protoplasm—is a substance quite like the simple proteins chemically.

The chemistry of the proteins is still a collection of facts which fail to reveal the quantitative formula, much less the structure of the molecule. The most trustworthy analysis of egg albumen is that of Franz Hofmeister (*Zeitsch. für physiol. Chemie*, 1892, Bd. xvi.), which resulted in the following formula:

$$\text{Egg albumen} = C_{204}H_{322}N_{52}O_{66}S_2.$$

Though this molecular formula for egg albumen may be modified by subsequent investigations, it serves to indicate (1) that typical proteins contain C, H, O, N, and S, and (2) that typical proteins are made up of exceedingly large and complex molecules.

Besides the elements above enumerated, some of the proteins (nucleoproteins) contain *phosphorus* and some (chromoproteins) contain *iron*.

The indiffusibility of most of the proteins may be due to the great size of the molecule.

The proteins are necessary constituents of animal food. There is a certain minimum protein requirement for every animal. If the food contain less than that, the animal must die of malnutrition. On the other hand, carbohydrates or fats or both of these may be withheld from an animal and no serious result will follow.

The reasons for these facts will be given later. The facts are mentioned here to impress the student with the great importance of the proteins in nutrition.

Certain chemical characteristics of the proteins will be mentioned in connection with their classification.

CLASSIFICATION OF PROTEINS.[1]

a. Proteins Proper.

1. **Albumins.**—Soluble in water; and in a saturated solution of $MgSO_4$ or $NaCl$, insoluble in a saturated solution of $(NH_4)_2SO_4$. The albumins are coagulated by moderate heat, 63° to 75° C., and respond typically to the xanthoproteic test, Millon's reagent, and

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[1] The Cohnheim-Hammarsten classification.

other *general* protein tests. The following native albumins may be given: (I) *Egg albumen*, precipitated by ether (Halliburton). (II) *Serum albumin*, not precipitated by ether (Halliburton). It is the principal protein constituent of blood plasma. (III) *Lactoalbumin* is one of the protein constituents of milk. When milk is boiled the lactoalbumin coagulates and collects upon the surface in a thin membrane. (IV) *Myoalbumin* is one of the proteins of muscle tissue. (V) *Vegetable albumin*, of which there may be several kinds.

2. **Globulins.**—Insoluble in water, in saturated solutions of $MgSO_4$, $NaCl$, and $(NH_4)_2SO_4$; but soluble in dilute NaCl solution: (I) *Serum globulin*, one of the proteins of blood plasma and of lymph. (II) *Fibrinogen* is the plasma or lymph protein which is coagulated or precipitated under the influence of fibrin ferment and the calcium salts. The coagulated form probably somewhat modified chemically is called *fibrin*. (III) *Myosinogen*, the principal protein of living muscles. It coagulates after death and is in its modified form called *myosin*. (IV) *Myoglobulin*, associated with myosinogen in the composition of muscle tissue. (V) *Globin*, one of the constituents of hæmoglobin. (VI) *Vegetable globulin;* there are probably several forms.

3. **Nucleoalbumins.**—This group has been called one of *phosphorized proteins*. They differ from the nucleoproteins in not yielding any of the purin bases on cleavage; nor do they contain nucleic acid. Examples are *casein* and *vitelline*.

b. Derived Proteins.

To this class belong all of those modified proteins which are derived from native or combined proteins by physiologic processes.

1. **Albuminates.**—These bodies are derived from the native proteins through the action of an acid or alkali. (I) *Acid albumin*, or *Syntonin*, formed in the stomach by the action of HCl or other acid upon a protein. (II) *Alkali albumin*, formed in the small intestine by the action of the alkaline pancreatic juice upon the simple proteins of the foods.

2. **Proteoses and Peptones.**—These substances are derived from native proteins, or from albuminates by hydrolysis, probably by a hydrolytic cleavage of proteins, especially of the albuminate derivatives of native proteins.

c. Proteids.

1. **Nucleoproteids.**—These bodies are native compounds of nucleinic acid with protein. The nucleinic acid contains phosphorus, hence all nucleoproteids contain phosphorus; some of them contain iron. An example is *cell nuclein*, the chief protein of the nuclei of animal and vegetable cells.

2. **Chromoproteids** are native compounds of a protein with an animal pigment: (i) *Hæmoglobin*, globin with hæmatin in a true chemical combination. The pigment is hæmatin which contains iron. (ii) *Histohæmatin*, tissue hæmatin, especially the hæmatin of muscle tissue; also called myohæmatin.

3. **Glucoproteids** are native compounds of protein with a carbohydrate or allied body.

(*α*) GLUCOPROTEIDS free from phosphorus: (i) Mucins; (ii) Mucoids; (iii) Colloid; (iv) Amyloid.

(*β*) PHOSPHOGLUCOPROTEIDS: (i) Ichthulin; (ii) Helicoproteid.

d. Albuminoids.

These substances are closely related chemically to the other proteins and are derived from the native proteins by metabolic processes.

1. **Native Albuminoids.**—These include those albuminoids which exist normally in the animal body. (i) *Collagen.* The substance of which white fibrous connective tissue is composed. It is also a constituent of bone and of cartilage. (ii) *Elastin.* The substance of which yellow, elastic fibres of connective tissue is formed. (iii) *Keratin.* The horny material which is characteristic of the corneous layer of the epidermis, of nails, hair, horns, hoofs, and feathers. Keratin has a much larger proportion of sulphur than other proteins have. *Neurokeratin* is found in the medullary sheath of nerves.

2. **Derived Albuminoids.**—This class contains one example, namely: (i) *Gelatin,* which is derived from *collagen* by hydration. It is an artificial product and is prepared by long boiling of any of the connective tissues of the animal body. The collagen, at first insoluble, becomes hydrated and soluble gelatin, which on cooling sets into a jelly. When the excess of water evaporates the mass is amorphous and vitreous. It is soluble in hot water, indiffusible, gives most of the general protein reactions, and, what is of great importance, is *digestible.* It follows the general course of protein digestion and is absorbed as gelatin peptone. This gelatin peptone can be katabolized in the tissues, but it cannot be built up into tissue protoplasm. Its importance in nutrition will be discussed under metabolism.

5. FERMENTS AND ENZYMES.

a. Ferments in General.

Every living cell has the power to cause chemical reactions. Food materials are absorbed by the cell and are either first built up into protoplasm by a series of anabolic reactions, to be later subjected to a series of katabolic reactions, or directly subjected to katabolism.

A tissue cell of a complex organism selects from the tissue plasma which surrounds the cell the materials which are to enter the series of metabolic changes. A unicellular organism selects the materials from the liquid or other medium which immediately surrounds it. The materials so selected may be called the cell foods. The foods selected by different one-celled organisms are as different as the heredity and environment of the organisms.

Whether or not the food must be built up into living protoplasm before it can be broken up into simpler bodies is still a matter of controversy. There is no doubt, however, that sooner or later all of the material absorbed by the living cell must be katabolized or broken up into simpler compounds.

After a certain number of katabolic changes the organism seems to have exhausted the energy of the material so far as it is capable of doing so. The final products of the katabolism (katabolites) are useless to the organism and are rejected (excreted). Among the katabolites are: CO_2, H_2O, NH_3, CH_4, H_2, H_2S.

These all represent compounds or elements whose energy is practically exhausted. There are many cell katabolites which are more or less complex and represent much energy: alcohol, acetic acid, butyric acid, etc.

Among the above-mentioned katabolites are several which are gaseous. If these gaseous materials are given off in sufficient quantities they escape in bubbles. If the unicellular organism, *e. g.*, the yeast cell, is living in nutrient fluid containing sugar—dextrose—it will take up the sugar, and will excrete alcohol and CO_2. The CO_2 escapes in gaseous form. The observation of this phenomenon gave rise to the term FERMENTATION. The organism which causes the fermentation is called a FERMENT. In the light of the chapters on general or cellular physiology and of the introductory statements above, it must be evident that *fermentation is a phase of cellular nutrition.* The term has been extended to include *all of those phases of the nutrition of unicellular organisms which involve the consumption of complex substances and the excretion of simpler ones.* The term *ferment* is applied to all the unicellular organisms which cause *fermentive* or *putrefactive* changes. As examples of these organisms one may enumerate: (I) The yeast plant, *Saccharomyces cerevisiæ*, which consumes sugar and excretes alcohol and CO_2. (II) The *Bacterium lactis*, which consumes milk-sugar and water and excretes lactic acid ($C_{12}H_{22}O_{11} + H_2O = 4C_3H_6O_3$. (III) The *Mycodermi aceti*, which consumes alcohol and oxygen and excretes acetic acid ($C_2H_6O + O = H_2O + C_2H_4O_2$). (IV) Pasteur's *Fermentum butyricum*, one of the vibriones, which consumes lactic acid, malic acid, tartaric acid, or mucic acid, and excretes *butyric acid*, with a combination of various accompaniments (CO_2, H_2O, H_2, or acetic acid) according to the food consumed. (V) The *Vibrios*, which consume protein matter and produce in a liquid containing it what is known as *putrid fermentation* or *putrefaction.* Among the excreta may be enumerated: leucin, tyrosin; formic, acetic, propionic, butyric, valerianic, caproic and caprylic acids; ammonia, ethylamine, propylamine, trimethylamine, CO_2, H_2S, H, and N.

All of the ferments enumerated above are micro-organisms, the saccharomyces being a unicellular fungus and the remaining examples being bacteria. These organisms, though perhaps less sensitive to variations in the supply of oxygen than most living things, nevertheless are much influenced in their activities by the presence of free oxygen. The subject was most exhaustively studied by Pasteur. Summing up his studies Pasteur said (*Comp.-rend. de l'Acad. des Sci.*, vol. lxxv. p. 784): "The weight of yeast which is produced under these conditions—*i. e.*, in the presence of free oxygen gas—during the decomposition of sugar increases progressively, and approaches the weight of the decomposed sugar, in exact proportion as its life goes on in the presence of increasing quantities of free oxygen gas.[1] Guided by these facts I have been gradually led to look upon fermentation as a necessary consequence of the manifestation of life when that life goes on without the direct combustion due to free oxygen. We may see as a consequence of this theory that *every organism, every cell which lives or continues its life without making use of atmospheric air, or which uses it in quantities insufficient for the whole of the phenomena of its own nutrition, must possess the characteristics of a ferment with regard to the substance which is the source of its total or complemental heat.*"

Thus saccharomyces supplements the energy liberated through oxidation of its own tissues with free atmospheric oxygen, by energy liberated through katabolism of sugar. Some organisms, notably the vibriones, dispense with atmospheric oxygen altogether, carrying on all their life activities with the energy liberated through the katabolism of proteins.

b. Enzymes.

In our discussion of ferments we have mentioned only elementary unicellular organisms. In every case the organisms recognized as ferments live in a fluid or semifluid medium. Their pabulum is readily absorbable by the organism. We come now, however, to the consideration of nature's method of adaptation to new conditions. In a grain of corn or barley the embryo plant is embedded in a quantity of starch stored up by the parent plant for the nourishment of the germinating plantlet. Though the food supply surrounds the embryo it is an insoluble and unabsorbable solid.

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[1] "In fermentation without oxygen the ratio between the sugar decomposed and the yeast formed is from 60 or 80 to 1, while in fermentation in the presence of oxygen it is only 4 or 10 to 1."

How is it to be made soluble and absorbable? *The cells of the embryo secrete diastase, which brings about the hydrolysis or hydrolytic cleavage of the starch molecules, changing them to dextrose, which is soluble and absorbable.* The plant kingdom abounds in similar examples. Diastase and similar substances are called ferments or *Enzymes*. Diastase is not alive; it is not organized, and has, therefore, been called an *unorganized ferment*. The distinction between an organized and an unorganized ferment, or between a ferment organism and an enzyme, may be more apparent than real. It is most probable that the distinction is simply one of location of the reaction—*i. e.*, (I) *intracellular fermentation* caused by an enzyme upon absorbed substances; (II) *extracellular fermentation* caused by an enzyme upon unabsorbed, unabsorbable substances.

But animal cells produce enzymes also. When solid food is taken into the alimentary tract it may be insoluble and unabsorbable, as is the case, for example, with starch and lean meat. Unless these foods be rendered soluble they will be useless to the organism. *Specialized cells along the alimentary canal secrete enzymes, which bring about the hydrolytic cleavage of the food molecules, changing them to forms which are soluble and absorbable.* The specialized cells in question do not absorb the products of fermentation (digestion). Other cells and specialized tissues absorb the nutriment, which is distributed throughout the organism by still other organs and tissues. The cells which secreted the enzyme finally receive their sustenance from the common treasury—the blood.

Enzymes may be classified as follows:

1. **Amylolytic Enzymes.**—*Diastase*, *Ptyalin*, *Amylopsin*, which change starch to maltose or dextrose, dextrin being an intermediate substance. The ultimate change wrought in the starch may be summed up in the following equations: $(C_6H_{10}O_5)_n + nH_2O = nC_6H_{12}O_6$, dextrose. The steps of this process have been studied by numerous investigators. Neumeister's results will be given later under Salivary Digestion. The steps of the process for ptyalin or amylopsin are probably, in a general way, typical of all enzyme action.

2. **Inverting Enzymes.**—The *Invertin* which the yeast plant secretes for splitting cane-sugar into dextrose and levulose may be cited as an example. A similar enzyme, secreted in the small intestine, changes cane-sugar and maltose to dextrose.

3. **Proteolytic Enzymes.**—The *Pepsin*, secreted in the stomach, and the *Trypsin*, secreted by the pancreas, represent this class. They act upon proteins, converting them into peptones through several intermediate steps.

4. **Lipolytic, or Fat-splitting Enzymes.**—An example of this is the *lipase* of the pancreatic juice. It acts upon fat, causing each molecule to take up three molecules of water and split into three molecules of fatty acid and one molecule of glycerin.

5. **Coagulating Enzymes.**—Such as *Rennin* and *Thrombin*, the first precipitating caseinogen as casein and the second precipitating fibrinogen as fibrin.

Note the radical difference between the first four classes of enzymes and the last class. The first four classes change insoluble substances to soluble ones; the fifth class changes soluble substances to insoluble ones.

c. Conditions of the Activity of Ferments and Enzymes.

(*α*) THE OPTIMUM TEMPERATURE is 35° C. to 40° C., while the maximum is below the boiling point, the enzymes being destroyed by boiling. The action of enzymes is progressively less as the temperature falls from the optimum, being completely suspended by a zero temperature.

(*β*) THE ENZYME IS NOT QUANTITATIVELY INVOLVED IN THE REACTION which it causes. The quantitative relations between AgCl precipitated from a solution of chlorides by a certain amount of $AgNO_3$ is definite and unvarying. Time is not a factor in the amount of AgCl thrown down. An enzyme, however, can work a greater change in two hours than in one. The smaller the amount of enzyme, the longer the time it will require to work a particular change. Just what part the enzyme plays in the reaction is unknown. If it enters into the reaction by being molecularly incorporated in certain stages of the process it is later disengaged in its original form and may repeat its hydrolytic change upon fresh molecules of the pabulum. This repetition is not without limit, however; the enzyme becomes exhausted after a while and is no longer able to excite the reaction.

(*γ*) THE INHIBITORY INFLUENCE OF THE ACCUMULATION OF THE PRODUCTS OF ENZYME ACTION.—Another condition of the action of an enzyme which is of the greatest importance to the higher organism is this: when peptones have reached a certain degree of concentration they stop the further action of the enzymes until the product already formed is removed (by absorption), when the enzyme resumes activity.

E. FOODSTUFFS AND FOODS.

1. DEFINITIONS.

Gould defines *foodstuffs:* "The materials that may be employed for the purpose of nourishment and tissue formation." The same lexicographer defines *foods:* "The substances ordinarily employed as aliments." This distinction is not as clear-cut in the definitions as it is in use.

The term *foodstuff* is employed as a generic term including all of those chemical compounds which may be employed for the nourishment, growth, and repair of the organism. Examples: starch, sugar, oil, albumin.

A *food* is an article of diet which may be composed of one or more foodstuffs: *Bread,* composed of starch, glutin, fat, inorganic salts, water, etc. *Beefsteak,* composed of various proteins, fats, inorganic salts, water, etc. *Potatoes,* composed of starch, proteins, salts, cellulose, and water.

2. CHEMICAL COMPOSITION OF MILK AND OF THE ANIMAL BODY.

How shall we obtain a comprehensive idea of foods and foodstuffs? Nature furnishes every young mammal with a food—milk—which most perfectly satisfies the requirements enumerated above, growth and repair, and whose analysis may give us a clue to the chemical characters that foodstuffs should possess:

Chemical analysis of milk.	**Water**						87.0 %
	Solids	**Organic**	**Proteins**	**Caseinogen** **Lactalbumin**			4.0 %
			Fats	**Olein**	0.43	**100 parts**	4.0 %
				Palmitin	0.33		
				Stearin	0.16		
				Butyrin, caproin, caprylin	0.07		
			Carbohydrates—lactose				4.4 %
		Inorganic: $CaHPO_4$, $CaCO_3$, $NaCl$, $MgCl_2$, etc.					0.6 %

When we compare the chemical constituents of the mammalian body with the chemical composition of that food—milk—which nature furnishes to young mammals, we find an exact correspondence in the general constituents—*i. e.*, each contains water in large proportion, proteins, fats, carbohydrates, and salts, composed largely of phosphates, chlorides, and carbonates. The most noticeable difference between the two lists is the great variety of proteins in the mammalian body, while there are only two or three varieties in milk. If, of a family of young mammals, a part be sacrificed to chemical analysis at birth and the rest after their period of growth on a milk diet, the results of the analysis will be practically identical qualitatively, but all of the constituents will be found much greater in quantity in those which have had the milk diet. Such an experiment demonstrates conclusively that out of a few kinds of proteins many kinds may be built up.

The following table giving the chemical constituents of the animal body will show what the carnivorous animal eats:

- Chemical composition of the animal body.
  - Water . . . . about 67 %
  - Solids
    - Organic
      - Proteins . .
        - Albumins . . . . .
          - Serum albumin.
          - Myoalbumin.
        - Globulins . . . . .
          - Serumglobulin.
          - Fibrinogen.
          - Myosin.
          - Myoglobulin.
          - Globin.
          - Crystallin.
        - Chromoproteids
          - Hæmoglobin.
          - Histohæmatin.
        - Nucleoproteids.
        - Albuminoids . . .
          - Collagen.
          - Elastin.
          - Keratin.
      - Fats . . . .
        - Palmitin.
        - Stearin.
        - Olein, etc.
      - Carbohydrates
        - Glycoses: dextrose.
        - Saccharoses: lactose during lactation.
        - Amyloses: glycogen.
    - Inorganic
      - NaCl, $CaHPO_4$, $CaCO_3$
      - KCl, $Ca_3(PO_4)_2$, Na_2CO_3
      - $MgCl_2$, Na_2HPO_4, $NaHCO_3$
      - $CaCl_2$, NaH_2PO_4.
      - Fe in organic combination in hæmatin and tissues in general.

As the next step in our discussion let us make a list of those ingested by a carnivorous animal. The wolf or fox catches and eats rabbits or birds. This food of the carnivorous animal has already been analyzed, and we see that it corresponds in every respect to the body which it must nourish. Our first and most natural thought is that the proteins of the rabbit become the proteins of the wolf, kind for kind—*i. e.*, the myosin or muscle protein of the rabbit becomes the muscle protein of the wolf. But this natural inference is fallacious. All proteins are, during digestion, reduced to peptones, from which, after absorption into the circulatory system, the various proteins of the carnivorous animals are built up. If there be an excess of protein in the blood this excess may be deposited in the changed form of fat. Further, the quality and quantity of fat in the wolf does not correspond to the quality and quantity of this constituent in the rabbit. The only inference possible is that the rabbit fat, after being taken up into the blood of the wolf, is partially consumed in some metabolic process and partially deposited, but the several constituents—olein, palmitin, and stearin—are deposited in a new proportion peculiar to the wolf. Similar observations and conclusions might be made regarding the carbohydrates. But where does the rabbit obtain this ample list of constituents? He does not get his food so nearly prepared as does the fox. He eats only herbaceous material—he is herbivorous. His diet of barks, vegetables, and tender, herbaceous shoots, if subjected to chemical analysis, will be found to contain, besides water, very large quantities of carbohydrates and very small quantities of fats and proteins. Among the carbohydrates the principal constituent is cellulose, though there is also a small quantity of glucose and starch. From these crude foodstuffs the herbivorous animal is able to build up all the complex proteins and fats of his body, while the carnivorous animal is quite unable to accomplish the first step in the digestion of cellulose.

3. CLASSIFICATION OF FOODSTUFFS.

- **Foodstuffs**
  - **Inorganic**
    - Water.
    - **Salts**
      - NaCl, KCl.
      - Na_2CO_3, K_2CO_3, $MgCO_3$.
      - Na_2SO_4, K_2SO_4, $MgSO_4$.
      - Na_2HPO_4, K_2HPO_4, $MgHPO_4$, $CaHPO_4$.
      - Na, K, Ca, etc., combined with fruit acids (tartaric, citric, malic, etc.).
      - Fe combined with animal proteids (hæmoglobin) and with vegetable compounds (chlorophyll).
  - **Organic**
    - **Carbonaceous**
      - **Carbohydrates**
        - Amyloses
          - Starch.
          - Glycogen.
          - Cellulose.
        - Saccharoses
          - Cane-sugar.
          - Lactose.
          - Maltose.
        - Glycoses
          - Dextrose.
          - Levulose.
          - Galactose.
      - **Fats**
        - Palmitin.
        - Stearin.
        - Olein.
    - **Nitrogenous**
      - Proteins
        - Albumins, Globulins, Nucleoproteids — Animal and vegetable varieties.
        - Chromoproteids.
        - Albuminoids, collagen, etc.
        - Derived albuminoid, gelatin.

4. FOODS.[1]

I. Inorganic Foods.

(*a*) **Water.**—Water comprises about 67 per cent. of the mammalian body. It is a general solvent and diluent. All of the secretions of the body are composed very largely of water. It is an absolutely indispensable food. An adult requires from 2000 c.c. to 2500 c.c. every twenty-four hours. Of this about one-third is taken in the form of liquid food (soup and beverages), leaving about 600 c.c. to 800 c.c. (three to four glasses) per day to be taken as "drinking water." Many people take much less water than this. "One of the most universal dietetic failings is neglect to take enough water into the system." (Thompson.)

One of the most important uses of water is as a *thermolytic* agent, regulating the body temperature through distributing the body heat, and through liberating heat from the surface of the body by evaporation of perspiration.

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[1] In the preparation of this section I have drawn freely upon Dr. W. Gilman Thompson's admirable work on Practical Dietetics.

(*b*) **Salts.**—Salts in general serve the following uses in the system:

1. "To regulate the specific gravity of the blood and other fluids of the body."
2. "To regulate the chemical reaction of the blood and the various secretions and excretions."
3. "To preserve the tissues from disorganization and putrefaction."
4. "To control the rate of absorption by osmosis."
5. "To enter into the permanent composition of certain structures, especially the bones and teeth."
6. "To enable the blood to hold certain materials in solution."
7. "To serve special purposes, such, for example, as the influence of sodium chloride on the formation of hydrochloric acid, and that of lime salts in favoring coagulation of the blood." (W. G. T.)

As a rule, little care need be given to the salts, because the vegetable and animal foods of a mixed diet all contain salts, making, when taken together, a list sufficient in quantity and quality, with the single exception of the sodium salts. Plants are especially rich in potassium salts and comparatively poor in sodium; thus herbivorous animals need more of the sodium salts, especially sodium chloride, than appears in the vegetable diet, and to this end eat earths rich in these salts—thus have been established the "deer-licks," visited by the herbivora of a whole region.

Carnivora seem to get a sufficient supply of the salts from the flesh of the herbivora which they consume. Omnivora need supplementary sodium salts in proportion to the part which vegetables play in their diet. Vegetarians need extra sodium chloride. Certain disturbances of nutrition (anæmia, etc.) arise from or result in a deficiency of certain minerals or mineral salts. A serious problem confronting the clinicians has been to determine the form of mineral nutriment best adapted to the animal organism suffering from malnutrition. Whether the needed salts should be given directly as such, or whether vegetable and animal foods rich in the needed salts should be made predominant in the diet, are the alternatives between which the clinicians wavered for many years. The general consensus of opinion, as expressed in practice, is in favor of the second alternative. Patients who need more iron are given eggs, lean meats, cereals, peas, beans, and "greens" rich in chlorophyll. Patients who need bone-making salts are given, among other foods, an abundance of milk, which contains calcium salts in a form and proportion which seem best adapted to the system.

II. Organic Foods.

In our classification of organic foods we must not lose sight of the fact that each one is usually a combination of several foodstuffs. In our grouping we shall have to be governed first by the predominating foodstuff, and, second, by the dietetic use of the food.

- Classification of foods
  - I. Inorganic
    - a. Water.
    - b. Salts.
  - II. Organic
    - a. Carbonaceous
      - 1. Sugars and syrups.
      - 2. Starches.
      - 3. Roots and tubers.
      - 4. Green vegetables.
      - 5. Fruits.
      - 6. Fats and oils.
    - b. Carbonitrogenous, or complete foods
      - 1. Cereals.
      - 2. Legumes.
      - 3. Milk.
      - 4. Nuts.
    - c. Nitrogenous
      - 1. Eggs.
      - 2. Meats.

a. Carbonaceous Foods.

1. **Sugars and Syrups.**—This general subclass of the carbohydrate foodstuffs has the great advantage that it requires little or no digestion, may be directly absorbed and very readily assimilated. The most common food-sugars are: *cane-sugar, glucose,* and *milk-sugar.* Cane-sugar, or saccharose, is derived from the sap of sugar-cane, beetroots, and maple trees. Glucose, or dextrose, is manufactured from starch, makes a prominent constituent of powdered sugar, and is used in the table syrups. It is the most common fruit and vegetable sugar; in grapes, cherries, figs, dates, bananas, onions, turnips, cabbage, etc.

Milk-sugar, or lactose, constitutes about 4 per cent. of cows' milk and is usually used only in milk. Honey is a natural syrup formed by flowers and collected by bees. König's analysis gives: water, 16.13 per cent.; fructose, 78.74 per cent.; saccharose, 2.69 per cent.; nitrogenous matter, 1.29 per cent.; salts, 0.12 per cent.

2. **Starches.**—*Tapioca* and arrowroot are prepared from the rootstalks of certain tropical and subtropical plants. *Sago* is extracted from the pith of certain tropical palms. Tapioca and sago are practically pure starch, while arrowroot contains H_2O 15.4 per cent., protein 0.8 per cent., and starch 83.3 per cent. *Corn starch* is 97.8 per cent. starch.

3. **Roots and Tubers.**—White potatoes, sweet potatoes, beets, carrots, parsnips, turnips, radishes, etc., represent this class of vegetable foods. All of this class are rich in salts, especially the salts of potassium. The nutrient portion of potatoes consists largely of starch; while in the other vegetables enumerated it consists chiefly of sugar.

The following table, combined from analyses by Letheby and by König, gives the nutrient values of the—

ROOTS AND TUBERS.

FOODS.	WATER.	PROTEINS	FATS.	SUGAR.	STARCH.	CELLULOSE.	SALTS.	ANALYST.
Potato (white)	75.0 %	2.10 %	0.2 %	3.2 %	18.8 %	......	0.7 %	Letheby.
Potato (sweet)	67.5	1.5	0.3	10.2	16.0	0.45 %	2.6	Payen.
Parsnips	82.0	1.1	0.5	5.8	9.6	......	1.0	Letheby.
Carrots	83.0	1.3	0.2	......	8.4	......	1.0	Letheby.
Onions	86.0	1.86	0.1	2.8	No starch "extractives" 8%	0.7	0.7	König.
Beet-root	87.1	1.4	......	0.6	......	1.0	0.9	König.
Turnips	91.2	1.0	0.2	4.1	"Extractives" 1.9	0.9	0.75	König.

All of the foods in the above table are preserved for use in winter, during which season the absence of green vegetables makes them especially desirable and palatable.

4. **Green Vegetables.**—These are used mostly "*in season.*" They represent very little nutriment, but serve rather to sharpen the appetite for heavier foods. Spinach is rich in iron and is an especially fine food for use when more iron should be introduced into the system.

Lettuce and celery both act as sedatives on the nervous system. Rhubarb has a laxative action, while asparagus acts as a diuretic. The following table gives analysis of a few of the more important green vegetables:

COMPOSITION OF GREEN VEGETABLES (König, quoted by W. G. T.).

FOOD.	WATER.	PROTEINS.	FATS.	SUGAR.	EXTRACTIVES.	CELLULOSE.	SALTS.
Celery	84.1 %	1.5 %	0.4%	0.8 %	11.0 %	1.4 %	0.8 %
Cabbage . . .	90.0	1.9	0.2	2.3	25.8	1 8	1.23
Cauliflower . .	90.4	2.5	0.4	1.3	23.7	0.9	0.8
Spinach . . .	90.3	3.2	0.5	0.1	23.3	0.8	1.94
Asparagus. . .	93.3	2.0	0.3	0.4	22.3	1.1	0.5
Lettuce	94.3	1.4	0.3	......	21.9	0.7	1.0

To this same class belong cucumbers, egg-plant, pumpkin, squash, and vegetable marrow.

5. **Fruits.**—The following table gives the composition of the principal fruits used in this country:

FRUITS.

FRUIT.	WATER.	NITROGENOUS MATTER.	SUGAR.	FREE ACIDS.		OTHER NON-NITROGENOUS MATTER.	CELLULOSE AND KERNEL.	SALTS.	ANALYST.
Apple.	83.6 %	0.4	7.7	0.8		5.2	2.0	0.8	Bauer.
Pear.	83.0	0.36	8.26	0.2		3.54	4.3	0.3	“
Peach.	83.0	0.65	4.5	0.9		7.2	6.06	0.7	“
Grape.	78.2	0.6	14.36	0.8		1.96	3.6	0.5	“
Strawberry.	87.66	1.1	6.3	0.9		0.5	2.3	0.8	“
Currant.	84.8	0.5	6.4	2.15		0.9	4.6	0.7	“
Orange pulp.	89.0	0.7	4.6	2.44		0.9	1.8	0.5	“
				FAT.					
Cherry.	49.9	2.1	32.2	0.3		14.3	0.6	1.6	Yeo.
Raisin.	32.0	2.4	57.26	0.5		7.5	1.7	1.2	“
				FAT.	ACID.				
Fig.	31.2	4.0	49.8	1.44	1.2	4.5	5.0	2.86	“

Thompson gives the following list of uses for fruits:

(*α*) "TO FURNISH NUTRIMENT."—The nutriment is chiefly found in the sugar. The most nutritious fruits are: fig, prune, grape, date, banana, cherry.

(*β*) "TO CONVEY WATER TO THE SYSTEM AND RELIEVE THIRST."—Besides melons, the orange, lemon, grape, and pear seem best adapted to this purpose.

(*γ*) "TO INTRODUCE VARIOUS SALTS AND ORGANIC ACIDS WHICH IMPROVE THE QUALITY OF THE BLOOD AND REACT FAVORABLY UPON THE SECRETION."—The salts of especial importance are citrate, tartrate, and malate of sodium and potassium. Citric acid and the citrates predominate in lemons and oranges; tartaric acid and the tartrates in grapes, and malic acid and the malates in apples, pears, peaches, apricots, gooseberries, currants (and rhubarb). The alkalinity of the blood and secretions is increased with a fruit diet, owing to the release of the K and Na from the organic acids and their combination as carbonates, phosphates, etc.

(The tomato is really a fruit, though in the diet it is associated with the green vegetables. It contains oxalic acid, which is injurious in uric acid diathesis).

(*δ*) TO SERVE AS THERAPEUTIC AGENTS.—(I) "*As antiscorbutics;* (II) *as diuretics;* (III) *as laxatives and cathartics.*" The antiscorbutic action of such fruits as apples, lemons, and oranges is due to their abundance of the salts of potassium, magnesium, and calcium. The diuretic action of fruits is due in part to the water which they contain. The citrates which oranges and lemons contain are especially stimulating to the action of the kidneys. The laxative action of fruits is best marked in apples, figs, prunes, dates, grapes, peaches, and berries.

(ε) Fruits "STIMULATE THE APPETITE, IMPROVE DIGESTION, AND GIVE VARIETY TO THE DIET." (Quotations from W. G. Thompson.)

6. **Fats and Oils.**—These important foods are found both in the vegetable and in the animal kingdom and may be considered here. Twenty per cent. of the normal body weight consists of fat. This is in small part derived directly from the fat of the food, but rather from the sugars and starches, with a small portion from the proteins. Most of the ingested fat is oxidized at once and supplies a considerable part of the animal heat. One may thus summarize the uses of the fats. The ingested fats serve:

(α) "TO FURNISH ENERGY FOR THE DEVELOPMENT OF HEAT."

(β) "TO SPARE THE TISSUES FROM DISINTEGRATION, for although their combustion in the body results largely in the production of heat, they also take part to some extent in tissue formation."

The deposited fats serve:

(γ) "TO STORE ENERGY IN POTENTIAL FORM."

(δ) "THROUGH THE SUBCUTANEOUS COAT OF ADIPOSE tissue, to conserve the heat of the body."

(ε) "TO LUBRICATE and make more plastic various structures of the body and give rotundity to the form." (Quotations from W. G. T.)

The most important vegetable oils are: *olive oil*, cotton-seed oil, used in dressings and cooking, and the oil of nuts.

Animal fats and oils are: *butter*, *cream*, *suet*, *lard*, and the fats of beef, mutton, pork, and fish. The yolk of eggs is also rich in oil.

b. Carbonitrogenous or Complete Foods.

1. **Cereals.**—These comprise grains, including wheat, corn, rice, rye, oats, barley. The cereals with potatoes form the most common source of starch. The cereals are usually used in the form of meal or flour. Not only do the cereals contain considerable proteins with some fats, but in the preparation of these meals and flours for eating it is customary to make important additions in the form of milk, eggs, and fat, so that the resulting preparation is a complex food which generally represents all of the foodstuffs in a proportion approaching that of a typical diet.

The following table illustrates this as far as it concerns bread and crackers:

COMPOSITION OF BREADS AND CRACKERS (Clark, quoted by Thompson).

FOOD.	WATER.	NUTRIENTS.	PROTEINS.	FATS.	CARBO-HYDRATES.	SALTS.
Wheat bread . .	32.5 %	67.5 %	8.8 %	1.9 %	55.8 %	1.0 %
Graham " . .	34.2	65.8	9.5	1.4	53.3	1.6
Rye " . .	30.0	70.0	8.4	0.5	59.7	1.4
Soda crackers .	8.0	92.0	10.8	9.4	70.5	1.8
Graham " . .	5.0	95.0	9.8	13.5	69.7	2.0
Oatmeal " . .	4.9	95.1	10.4	13.7	69.6	1.4
Oyster " . .	3.8	96.2	11.3	4.8	77.5	2.6
Graham bread nutrients	......	100.0	14.8	22.2	83.7	To compare the nutrients of Graham bread with a typical diet.
Typical diet nutriment	......	100.0	17.5	8.4	73.8	

COMPOSITION OF VARIOUS FOODS OF CLASSES *a* AND *b*.

FOOD.	WATER.	PROTEINS.	FATS.	CARBO-HYDRATES.	SALTS.	ENERGY IN KILO-CALORIES PER LB.
Sugar	2.0 %	......	......	97.8 %	0.2 %	1820 calories.
Syrup	43.7	......	......	55.0	2.3	1023 "
Tapioca, Corn starch . .	2.0	......	......	97.8	0.2	1820 "
Rice	12.4	7.4 %	0.4 %	79.4	0.4	1630 "
Macaroni . . .	13.1	9.0	0.3	76.8	0.8	1406 "
Flour	12.5	11.0	1.0	74.9	0.5	1644 "
Corn meal . . .	15.0	9.2	3.8	70.6	1.4	1645 "
Oatmeal	7.6	15.1	7.1	68.2	2.0	1850 "
Beans or peas . .	12.6	23.1	2.0	59.2	3.1	1615 "
Potatoes	78.9	2.1	0.1	17.9	1.0	375 "
Onions	87.6	1.4	0.3	10.1	0.6	225 "
Cabbage . . .	92.0	2.1	0.6	5.5	1.1	155 "

2. **Legumes.**—Beans and peas contain, besides a large amount of starch, so large a proportion of proteins that they may be used as one of the recognized sources of proteins, though the animal foods form the most important source of proteins.

3. **Milk.**—One analysis of cows' milk (Bunge's) was given at the head of this section.

The following table gives the analysis of cows' milk and human milk by A. H. Leeds. (Quoted from W. G. Thompson.)

	"Sound Dairy Milk."	Human Milk.
Reaction	Faintly acid	Alkaline.
Specific gravity	1029.7	1031.3
Bacteria	Always present	Absent.
Fats	3.75%	4.13%
Lactose	4.42	7.0
Proteins	3.76	2.0
Salts	0.68	0.2
Total solids	12.61	13.33
Water	87.39	86.67

Thompson enumerates the following as "the more important uses of milk":

(*a*) Purely as Food: (i) "*As Infant Food.*"

(ii) "*As a Food for Adults.*"

(iii) "*As a Source* of special food products and derivatives, such as cream, butter, cheese, buttermilk, koumiss."

(iv) "*As a Most Important Constituent* in various composite foods, as bread, omelet," etc.

(v) "*As a Vehicle* for the administration of other foods for invalids —*e. g.*, egg albumen, beef meal, cocoa, meat juice, peptonoids," etc.

(*β*) Therapeutic Uses of Milk: (i) "*As a Diuretic.*"

(ii) "*For its Soothing Effect* on diseased mucous membranes of the alimentary canal."

(iii) "*To Loosen a Cough* (when given hot)."

(iv) "*For Rectal Injection,*" really a food in this case.

(v) "*As a Vehicle* for the administration of medicines. The following table gives the constituents of the more important derivatives of milk":

Food.	Water.	Proteins.	Fats.	Sugar.	Salts.	Analyst.
Milk	86.8 %	4.0 %	3.7 %	4.8 %	0.7 %	Parkes.
Skimmed milk	88.0	4.0	1.8	5.4	0.8	"
Cream	66.0	2.7	26.7	2.8	1.8	"
Cheese	36.8	33.5	24.3	......	5.4	"
Butter	6.0	0.3	91.0	......	2.7	"

c. Nitrogenous Foods.

1. **Eggs.**—Milk is nature's food for young mammals, and eggs are nature's food for young birds. Both of these natural foods contain all

of the foodstuffs necessary for a developing animal. Bauer gives the average weight of the hen's egg as 50 gms., of which the shell represents 7 gms., or 14 per cent.; the white 27 gms., or 54 per cent., and the yolk 16 gms., or 32 per cent. Parkes allows only 10 per cent. of the weight for the shell, the yolk and white together being composed of: water, 73.5 per cent.; proteins, 13.5 per cent.; fats, 11.6 per cent.; salts, 1 per cent.

Eggs represent a concentrated diet, and though they contain considerable fat, they are classed as a *protein food.* Egg albumen digests more easily in the natural uncooked state than when coagulated by cooking. Raw eggs are, however, quite unpalatable to most people, and it is customary to cook them. Egg albumen begins to coagulate at 56.5° C. (about 134° F.) and the process progresses to about 70° C. (or 160° F.). If the temperature is raised to the boiling point the albumen becomes very densely coagulated and difficult of digestion. The most prevalent method of eating eggs is in various milk compounds: omelets, custards, etc.

This mixing of the egg with milk seems to correct the difficulty of indigestible coagula, besides making a most palatable food.

2. **Meats.**—We generally rely upon the lean meat of various animals for our supply of proteins, though it must not be forgotten that many of the cereals and the legumes contain a very large proportion of proteins—a proportion quite sufficient to ensure the proper nutrition of the body without resort to the addition of lean meats. The variety which is given by the addition of meats to the diet would justify it, however, even if there were no other reasons favorable to it. Liebig said: "It is certain that three men, one of whom has had a full meal of meat and bread, the second cheese or salt fish (and bread), and the third potatoes, regard a difficulty which presents itself from entirely different points of view." The aggressive peoples of northern Europe and the western continent are the meat-eating people of the world. Besides overcoming the very great difficulties of a northern climate they have outstripped their vegetarian competitors in almost every field of human endeavor. Just what gives to a meat diet this subtle influence is a problem. That the influence exists is not a matter of controversy. In its extremes we see the difference in meat and vegetable diet wrought upon the lion and the ox: the vegetarian, though strong, is slow, clumsy, and lazy; the meat-eater quick, graceful, and alert.

The author does not wish to be understood to approve of an exclusively meat diet. Man is omnivorous. If meat makes too great a proportion of his diet, disturbances of nutrition are almost sure to manifest themselves. Generally speaking, Americans and Englishmen eat rather too much meat.

We need meat, but we do not need it in immoderate quantities.

The following table gives the composition of some of the more common meats (including fish and "shell-fish"):

FOOD.	WATER.	PROTEIDS.	FAT.	CARBO-HYDRATES.	SALTS.	ANALYST.
Beefsteak.	74.4	20.5	3.5	——	1.6	Parkes.
Fat beef.	51.	14.8	29.8	——	4.4	Pavy.
Lean beef.	72.	19.3	3.6	——	5.1	"
Fat mutton.	53.	12.4	31.1	——	3.5	"
Lean mutton	72	18.3	4.9	——	4.8	"
Veal.	63	16.5	15.8	——	4.7	"
Fat pork.	39	9.8	48.9	——	2.3	"
Bacon.	15	8.8	73.3	——	2.9	"
Smoked ham.	27.0	34.0	36.0	——	10.0	Parkes.
Calves' liver.	72.8	20.1	5.6	——	1.5	Payen.
Poultry.	74.	21.	3.8	——	1.2	Parkes.
White fish.	78.	18.	2.9	——	1.	Parkes.
Canned salmon.	63.6	21.6	13.4	——	1.4	Woodford.
Crabs.	84.	15.	1.0	——	?.	"
Oysters.	87.	6.	1.2	3.7	2.	"

5. FOOD ACCESSORIES.

There are many substances which are taken with the food and which influence considerably the processes of nutrition, but which are not foods.

These substances are called *food accessories*, and may be classified as follows:

(*a*) **Beverages** are drinks which represent aqueous solutions or dilutions of various organic, usually vegetable, products: *tea, coffee, cocoa, chocolate, lemonade*, and allied drinks are examples. They serve to *relieve thirst*, as *nutrients*, as *diuretics*, as *diaphoretics*, or as *stimulants*.

(*b*) **Condiments** are substances added to food to give it a flavor or to modify its flavor. Examples are: *pepper, nutmeg, cinnamon, cloves, allspice, sage, thyme, mustard, ginger, mace, horseradish, vanilla, dill*, etc. The active principle in each of these is a volatile oil peculiar to the substance. These volatile oils have no importance as foods, but they serve as stimulants to the buccal mucous membrane and in that way frequently serve a good purpose in inciting a free flowing of the digestive juices.

(*c*) **Intoxicants** are beverages such as cider, beer, ale, wine, brandy, etc., the active principle of which is ethyl alcohol. Ethyl alcohol possesses several characteristics in common with the carbonaceous foods—*e.g.*, (I) it is composed of C, H, and O; (II) it is readily oxidized in the liver, yielding CO_2 and H_2O, which are excreted; (III) it yields heat incident to its oxidation, and this heat naturally augments the body income of heat; (IV) ingestion of ethyl alcohol leads to a decrease in the katabolism of carbonaceous foods and may even "spare" proteins.

In this connection one must not lose sight of the following facts:

(I) All vegetable toxins and alkaloids are composed of the same kind of chemical elements as enter into foodstuffs—viz., C, H, O, and N.

(II) Toxins and alkaloidal poisons in general are oxidized in the liver, through the agency of oxidases, whose function is to oxidize and thus make harmless substances which would act as protoplasmic poisons on all cells with which they come into contact. When moderate amounts of such toxins are taken the defences of the system are sufficient to reduce them to a harmless condition and no immediate injury results. If larger quantities are ingested the full drug effect (*narcotic* in the case of alcohol) is immediately experienced, the oxidases of the system being unable to defend it against a large dose.

(III) All oxidation yields heat, whether it is a normal katabolism or a protective oxidation. That the heat from the oxidation of alcohol is not a normal katabolism for the purpose of heat liberation is evident from the fact that, notwithstanding the liberation of heat on oxidation of alcohol, the temperature of the body falls, because of increased loss of heat from the surface. This increased loss is due to dilatation of peripheral vessels.

(IV) Decreased katabolism of carbonaceous or nitrogenous foods following ingestion of a narcotic is a universal fact depending upon the drug effect and giving to the oxidized narcotic no significance as a food. It may be said without reservation that ethyl alcohol is not a food in the full, scientific significance of the word.

6. PREPARATION OF FOODS.

Thompson says that "it is owing to the practice of cookery that the dietary of civilized man has been so much enlarged, and that it covers a wider range of materials than that which serves for the nourishment of lower animals."

The cooking of food serves the following purposes: (I) To render the organized structure of such foods as meats and vegetables more tender; therefore, more easy to masticate and to digest. (II) To render the foods more palatable through the flavors developed in cooking. Important as this is to those who have been used to cooked foods, it is easy to see that it might be quite unimportant to the savage; the Eskimo, for example, seems to prefer his meat raw. (III) To kill any parasites and germs which may be in the food as received from the market.

The cooking is accomplished in the following general ways: (I) boiling; (II) stewing; (III) steaming; (IV) frying; (V) baking; (VI) roasting and broiling.

(*a*) **In Boiling and Stewing** the cooking is conducted at a temperature which does not exceed 100° C. (212° F.). The two processes differ in this way: The food to be boiled is *plunged into boiling water;* this coagulates or hardens the surface, thus retaining within the mass the juices. The food to be stewed is put into cold water and the whole brought gradually to a boiling temperature; this process tends to extract the juices and to macerate the tissues somewhat. During the period of cooking which follows the above-described preliminary, the two processes consist alike in keeping the temperature at 100° C. In *steaming* the food is subjected to the steam which escapes from water boiling in an unsealed receptacle. The steam does not exceed 100° C. The effect is quite like that of boiling.

(*b*) **In Frying** the heat is transmitted to the food through the medium of heated fat or oil. Fats used in cooking may be heated to 400° F. before they begin to smoke. The food cooks therefore much more rapidly with this process than with those above described. The fat may sear the outside of the food or may permeate it to a greater or less extent. In any case the digestibility is somewhat decreased; in some cases it may be very much so.

(*c*) **In Baking, Roasting, and Broiling** the heat, as it radiates from coals or from stone or metal surfaces, is applied direct to the food.

The temperature may thus be much higher than that of boiling water.

In a general way it may be said: (I) That all foods that are cooked at all should be kept at 100° C. long enough to destroy parasites and bacteria. (II) That eggs, unless incorporated as constituents in composite foods, should be cooked as little as possible, the less the better. (III) That starchy foods should be very thoroughly cooked. (IV) That meats in general should be cooked just long enough to develop the flavors most agreeable to the recipient.

PHYSIOLOGY OF DIGESTION.

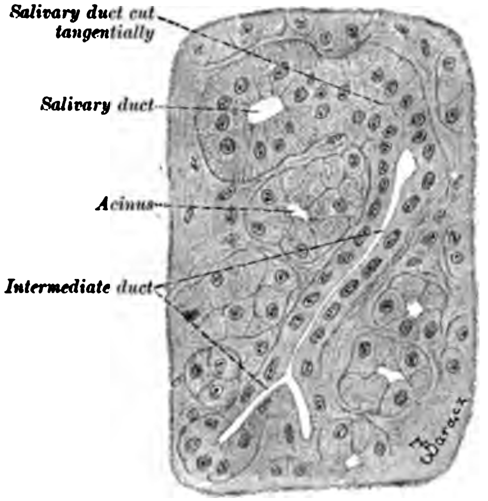
A. SALIVARY DIGESTION.

1. THE SALIVA.

a. The Secretion of Saliva.

The term *saliva* is applied to the fluid secreted into the oral cavity. There are three principal pairs of glands whose secretion forms a part of the saliva: the *parotids*, the *submaxillary*, and the *sublingual*. Besides these six glands there are innumerable smaller mucous glands whose secretion serves only to moisten the surfaces of the membrane, while the secretion of the salivary glands proper serves especially to moisten the food during mastication and to add to it a digestive ferment. These glands may be divided into two classes on the basis of the morphologic changes which the cells of the glands undergo during the period of rest and activity. Fig. 169 shows the cells of serous glands, the parotid, while Fig. 170 shows the cells of a mucous gland, the submaxillary. Note that the cells of the *serous* parotid gland are subspherical and nearly fill the alveolus, leaving a narrow,

FIG. 169



Section through a human parotid gland. (Szymonowicz.)

FIG. 170

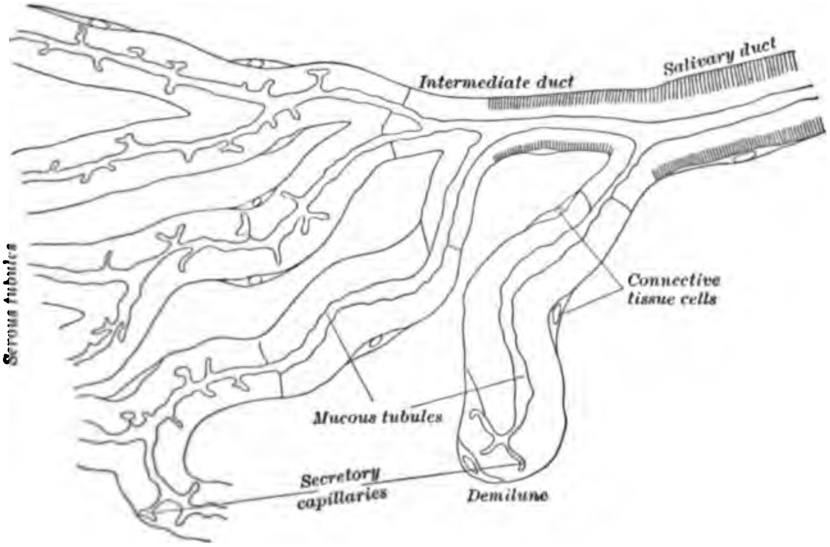
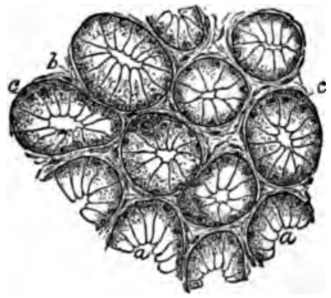


Diagram of a human submaxillary gland. (Szymonowicz.)

intercellular cleft, which widens into a definite lumen when the cells are depleted by secretion. The nucleus is located in the centre of the cell, but is obscured at times by the numerous granules. The granules vary in number during the different stages of the cell's rest and activity. They accumulate during rest and disappear during activity. The same general observation may be made upon the secreting cells of all of the digestive glands. The serous cells take the protoplasm stain, carmine, very deeply. The secretion from a serous gland is thin and watery. The cells of the *mucous*, sublingual gland, on the other hand, are pyramidal in shape. A distinct lumen always exists in the alveolus. The nucleus is located near the outer end of the cell. The general appearance of the resting, mucous cell is much less opaque than that of the resting, serous cell. There are, however, numerous granules, but these are less abundant near the lumen of the alveolus and more abundant in the neighborhood of the nuclei. This is well shown in Piersol's figure (Fig. 171). Just what is the significance of the demilunes of Heidenhain is still a matter of controversy. They may represent exhausted cells, pushed to one side by the active cells; or they may represent nascent cells, which are destined to take the place of cells which lie nearer to the lumen.

FIG. 171



Mucous acini of human lingual gland: the secreting cells (*a*), being loaded with the slightly staining secretion, appear clear and transparent; *c*, *c*, crescentic masses of granular cells—the demilunes of Heidenhain; *b*, interacinous connective tissue (After Piersol.)

The fact of greatest significance to the physiologist is the accumulation of granules in the gland cells during rest, and their disappearance during activity. That these granules bear some relation to the organic constituents of the secretion of the cells can be accepted as beyond question. Just what that relation is has not yet been definitely determined. The principal organic constituents of the saliva are mucin, ptyalin, and albumin. The work of Langley[1] upon the fresh gland shows that the granules of the mucus-secreting cell may be converted into mucin by simple addition of water. There can be no doubt that such a change takes place during secretion. The granules of the mucous cells may then be looked upon as the mother of mucin—*mucinogen*. The granules of the ptyalin-secreting cells probably represent the mother-substance of ptyalin. But the changes which take place in the cell during secretion are not confined to the solution of the granules and the expulsion of the product into the lumen of the alveolus. Extensive anabolic processes take place.

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[1] Journal of Physiology, vol. x. p. 433.

The cytoplasm is replenished and the increase in size of the nucleus indicates that the nucleoplasm is replenished also. During the resting stage the protoplasm undergoes a change, probably katabolic, by which the granules are again formed and the cell becomes "loaded," ready for another period of secretion.

This cycle of cell activity is controlled by influences outside of the cell. It is important for the organism that all of the secreting cells of a gland act in harmony, and that the secretory phase of the activity occurs at the time when food is in process of mastication. The co-ordination of the activity of the gland with the associated functions can only be brought about by the agency of the nervous system.

The nerve supply of the salivary glands represents two general sources: (I) cranial; (II) sympathetic.

The cranial innervation of the salivary glands is represented in the parotid gland by branches received directly from the auriculotemporal branch of the inferior maxillary division of the V cranial nerve. But these fibres come ultimately from the *glossopharyngeal* or IX cranial nerve and pass from that nerve to the auriculotempora through the tympanic nerve, the small superficial petrosal, and the otic ganglion. The cranial innervation of the submaxillary and sublingual glands is represented by branches received directly from the lingual branch of the inferior maxillary division of the V cranial nerve. These fibres come ultimately from the facial or VII cranial nerve and pass from that nerve to the lingual through the *chorda tympani*, so called because it traverses the tympanic cavity. (See Tympanum, under Hearing.)

The sympathetic innervation of the salivary glands is represented by branches from the superior cervical ganglion of the sympathetic system. These branches reach the glands by following the blood-vessels.

In a general way one may say that the nerve supply of all the digestive glands is derived, like that of the salivary glands, from cranial and sympathetic sources. A study of Fig. 160, giving the innervation of the digestive system, shows that this is true of the innervation of the stomach, of the small intestine, of the liver, and of the pancreas. The points which the innervation of the salivary glands possess in common with that of the other digestive glands, together with the fact that the nerves which supply the salivary glands are readily accessible to experimentation, has led physiologists to experiment extensively upon the influence of stimulation upon these glands, with a view to thus getting a clue to the influence of the nervous system upon secretion in general. The results are definite and conclusive with respect to the salivary glands themselves, and suggestive with respect to digestive glands in general. When we come to review the recent work of the Pawlow Institute we shall find not only a striking parallelism in the innervation of the several digestive organs, but a remarkable co-ordination in their work.

If the *chorda tympani* be severed and its distal end electrically stimulated, one may observe: (I) a dilatation of the bloodvessels and (II) a profuse flow of thin, watery saliva from the glands which it supplies. If the sympathetic branches to these glands be severed and electrically stimulated, one may observe: (I) a contraction of the bloodvessels and (II) a scanty secretion of thick, viscid saliva. In the case of the parotid gland, stimulation of the peripheral end of the divided parotid portion of the glossopharyngeal in any part of its course causes: (I) vasodilatation and (II) profuse watery secretion, while stimulation of the peripheral end of the divided sympathetic branches to that gland causes vasoconstriction, but, in most animals, no secretion of saliva.

Various theories have been advanced to account for the phenomena observed and to harmonize the results of physiologic experiments with the observations of the histologic changes in the gland cells during the cycle of cell activity.

That the increased pressure of the tissue plasma resulting from the vasodilatation bears an important relation to the pouring out of a watery secretion by the cells has been generally accepted since the time of Ludwig's early experiments in this field in 1851.

The theory which presents itself at once is that the water and salts of the secretion are products of filtration from the tissue plasma. If this be a tenable proposition, two things must be observed: first, that the proportion of water and salts in the saliva must be the same as in the tissue plasma: second, that the pressure of the secretion in the ducts of the gland will be less than the pressure of the blood in the vessels of the gland. But the water and the salts of the secretion are far different in proportion—the water and salts of the plasma being about 90.3 per cent. and 0.85 per cent. respectively, while they occur in the secretion in the proportions of 99.4 + and 0.36.

As to the pressure, Ludwig[1] found in the same experiment a blood pressure in the carotid artery of 112 mm. of mercury and a secretory pressure in the duct of the submaxillary rising to 190 mm. of mercury pressure when the gland is influenced by stimulation of the chorda tympani. Heidenhain[2] found even greater differences between blood pressure and secretory pressure. In the light of these observations it is evident that *the secretion of water and salts is not a process of filtration*. The next question which presents itself is: Do not the laws of diffusion and osmosis supplement and reinforce those of filtration?

The two most important factors in osmosis are: (I) The quantitative composition of the solutions separated by the membrane, and consequently the partial osmotic pressure exerted by the several constituents.[1] (II) The coefficients of diffusion of the various constituents. (Reid.) The first one of these two factors operates in the following manner: If pure water be separated by a membrane from a solution of sodium chloride the water will diffuse much more rapidly toward the salt solution than will the salt solution toward the water, so that the liquid will rise on the side of the denser liquid. The process of interchange continues until the liquid on both sides of the membrane has the same quantitative composition. But during the progress of salivary secretion water passes constantly from the plasma, where it forms only 90.3 per cent. of the liquid, into the alveoli of the salivary glands, where it forms 99.4 per cent. of the liquid.

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[1] Zeitsch. f. rat. Med., 1851, S. 271.

[2] Stud. d. physiol. Inst. zu Breslau.

It might be urged that the hydrostatic pressure overcomes any osmotic pressure that may exist on the opposite sides of the secreting cells. But we are seeking a factor to reinforce the hydrostatic pressure which was already too low to account for the secretory pressure. It is evident that the laws of osmosis will not assist us in accounting for the phenomena. To test the second factor of osmosis, the coefficients of diffusion of the various constituents, one may take for example a comparison of the two salts NaCl and KCl, both of which are constituents of both plasma and saliva. NaCl forms 0.55 per cent. and KCl, 0.03 per cent. of plasma. The coefficient of diffusion of KCl is nearly $\frac{3}{2}$ that of NaCl. Maeignae[2] demonstrated that *the rapidity of diffusion of the more diffusible of a pair of salts diffusing simultaneously is found to be increased, that of the less diffusible diminished* (Reid). For example, NaCl has about $\frac{5}{3}$ times the diffusibility of Na_2SO_4 when diffusing separately; when diffusing simultaneously the NaCl is increased and the Na_2SO_4 diminished, the ratio being nearly 3 : 1.

If a similar relation holds for NaCl and KCl in salivary secretion we shall be prepared to find in the saliva that the KCl, instead of being $\frac{1}{18}$ of the NaCl is increased to, say, $\frac{1}{12}$ or even $\frac{1}{10}$. But in the saliva the KCl : NaCl : : 3 : 5 (!).

When the two principal factors of osmosis are considered they are found to be completely inadequate to account for the phenomena of salivary secretion. The other factors of osmosis—character of membrane, pressure, temperature—are naturally the same for both salts and drop out of this calculation. We are forced to a further conclusion that: *the secretion of the water and the salts of the saliva is not a process of osmosis.* Finally: *the secretion of the water and the salts* of the saliva cannot be accounted for through the combined influence of the laws of *filtration* and the laws of *osmosis*. But these are the only known physical laws that may apply to this case.

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[1] Reid, in Schafer's Text-book of Physiology, vol. i. p. 278.

[2] Ann. de Chim., Paris, 1874, T. ii. p. 546.

The cells which separate the plasma from the saliva are living cells. *Every living cell undergoes metabolic changes;* building up a portion of the material, taken from the medium in which the cell exists, into protoplasm and retaining a portion as cell plasma or cell sap. *Every living cell has the power to select,* from the medium in which the cell exists, *the materials which are to be used by the cell in its metabolism.* In a complex organism the cells comprising the different tissues are differentiated in function. A differentiation of function involves a differentiation of cell metabolism with all that that entails. In terms of these fundamental principles of biology one may say that the cells of the salivary glands receive from the organism nutriment and protection while they give to the organism the results of specialized activity. The selection of particular constituents in particular proportion and the throwing out of a particular mixture of katabolites (excretions) are nothing new; but an attribute of every living cell. This is no attempt to tell just how the cell accomplishes this feat. The phenomenon is as inexplicable as life itself. This is an attempt to show that in the formation of a special secretion we have to deal with no new manifestation of cell life, but with a slight specialization of inherent cell attributes.

Of the various theories advanced to account for the phenomena of salivary secretion, that of Heidenhain as modified by Langley seems to be most reasonable. The essential features of this theory may be thus summarized:

(α) THE CRANIAL NERVES *supply the glands with vasodilator fibres and with secretory fibres.* In harmony with this hypothesis is the fact that if atropine be injected into the gland stimulation of the chorda tympani will cause no secretion, though the vasodilatation leads to increased vascularity of the gland.

The secretory fibres have been paralyzed by the atropine.

(β) THE SYMPATHETIC NERVES *supply the glands with vasoconstrictor fibres and with secretory (trophic) fibres.*

(γ) THE SECRETORY FIBRES, or at least secretory impulses, *may be classified as: (1) those which control the secretion of water and salts; (2) those trophic fibres which control the metabolism of the cells: (I) anabolic secretory, (II) katabolic secretory.*

In the dog the cranial nerve contains many fibres of class (1) and a few of class (2), while the sympathetic contains many of class (2) and a few or none of class (1).

To get a connected idea of the cycle of activity of the salivary gland let us begin with the period of rest or recuperation. (I) The reflex influence of the cranial nerves is suspended because the sensory nerves of the mouth are no longer stimulated by the presence of food and the process of mastication. (II) With suspension of the activity of the vasodilator fibres the general and practically constant vasoconstrictor impulses through the sympathetic nerves reduces the blood supply to the gland. (III) The katabolic impulses cause the cells to change some of the protoplasm, both cytoplasm and nucleoplasm, to those granular forms which, during the secreting period, may be so readily changed to constituents of the secretion. (IV) Anabolic impulses are unquestionably received by the cell during the resting stage, but the very great production of granules and the noticeable depletion of both cytoplasm and nucleoplasm makes it likely that the katabolic processes preponderate.

Consider now the changes which are wrought during the secreting period: (I) The reflex influence of the cranial nerves is brought into action through the stimulation of various sensory nerves, those of the nose and mouth predominating, and vasodilatation results. (II) Along with the increased blood supply come impulses through those secretory nerves which control the secretion of water and of salts. The increased pressure of the tissue plasma as well as the increased quantity of the tissue plasma facilitates this phase of the secretory activity of the cells, and they "*select*" certain proportions of water and salts and pass them into the lumen of the alveolus. (III) Through the sympathetic system come katabolic impulses which lead to the final step of katabolism necessary to change the granular material to the stage represented in the secretion. For example, mucinogen granules are changed to mucin, and the ptyalin granules (ptyalinogen) to ptyalin. (IV) Through the sympathetic system come anabolic impulses which cause the cell to select nutrient materials from the abundant plasma and replenish cytoplasm and nucleoplasm, the former collecting in the form of clear, non-granular protoplasm at the base of the cell, while the latter fills out the somewhat shrunken nucleus.

This presentation, based upon the Heidenhain theory, must be understood as a purely tentative one. It seems to harmonize all of the phenomena as now understood.

b. The Composition of Saliva.

Hammerbacher[1] gives the following analysis of human mixed saliva:

Human mixed saliva	**Water**			99.42 %
	Solids 0.58 %	**Organic**	**Mucin and epithelium**	0.22
			Ptyalin and globulin	0.14
			(Potassium sulphocyanide 0.004 %)	
		Inorganic	NaCl, KCl Na_2CO_3, $CaCO_3$ $Mg_3(PO_4)_2$, $Ca_3(PO_4)_2$	0.22
				100.00

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[1] Zeitsch. f. physiol. Chem., Bd. v.

2. THE CHEMISTRY OF SALIVARY DIGESTION.

The only chemically active agent in saliva is ptyalin. Ptyalin is an amylolytic enzyme, and its action is, therefore, confined to the change of starch to sugar and to the products intermediate between starch and sugar.

Under the influence of ptyalin and water the starch is subjected to a series of cleavages. Cleavages in general may be subdivided into two classes, *co-ordinate* and *subordinate*. In the former the molecule is broken up into two or more similar molecules; in the latter the original molecule is broken up into two molecules; but one of these is large and the other is small. It is as if the small molecule were split off from the side of the large one.

The cleavage of the starch molecule is a subordinate one, and according to Linterer and Dull[1] is represented by the following reactions:

(I) Starch $(C_6H_{10}O_5)n$ + Ptyalin = Amylodextrin $(C_{12}H_{20}O_{10})_{54}$.

(II) $(C_{12}H_{20}O_{10})_{54} + 3H_2O = 3[(C_{12}H_{20}O_{10})\cdot C_{12}H_{22}O_{11}]$.
Amylodextrin + Water = Erythrodextrin.

(III) $3[(C_{12}H_{20}O_{10})_{17}\cdot C_{12}H_{22}O_{11}] + 6H_2O = 9[(C_{12}H_{20}O_{10})_5\cdot C_{12}H_{22}O_{11}]$.
Erythrodextrin + Water = Achroödextrin.

(IV) $9[(C_{12}H_{20}O_{11})_5\cdot C_{12}H_{22}O_{11}] + 45H_2O = 54C_{12}H_{22}O_{11})$; or,
Achroödextrin + Water = Isomaltose = Maltose.

Neumeister looks upon the $C_{12}H_{22}O_{11}$ which appears in (II) as a separate maltose molecule. Note that a similar molecule is cleft off from the dextrin at each step. The last reaction represents a co-ordinate cleavage of each of the achroödextrin molecules into five isomaltose molecules.

The changes which glycogen $(C_6H_{10}O_5)_n$ undergoes during digestion are the same as those which starch undergoes.[2]

It must be remembered that though ptyalin is capable of working all of the changes ascribed to it when the time is sufficient, the amylolytic changes are interrupted very early in their course by the acid reaction of the stomach and are not resumed until the products are again subjected to the influence of an amylolytic enzyme in the small intestine. Under the usual conditions the products of ptyalin digestion would include maltose, achroödextrin, erythrodextrin, and probably amylodextrin; there would also remain much unchanged starch. All of these excepting the starch are soluble, and maltose is crystalline and diffusible. It is either hydrated in the alimentary canal by invertin, or an allied enzyme, and changed to dextrose, in which form it is absorbed; or it is taken up by the absorptive epithelium as maltose and changes within the epithelium to dextrose, in which form it passes into the capillaries of the portal system. It is certain that it does not enter the circulation as maltose.

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[1] Ber. d. Deutsch. chem. Gesell., Bd. xxvi., S. 2533.

[2] Kulz and Vogel, in Zeitsch. f. Biologie, 1895, Bd. xxxi., S. 108.

3. FACTORS WHICH INFLUENCE SALIVARY DIGESTION.

1. **The Preparation of the Food.**—The importance of a most thorough cooking of starch and starchy foods can scarcely be too strongly emphasized.

The starch is deposited in stratified grains which have alternating layers of pure starch or granulose and of starch cellulose, which also forms the outer layer of the starch grain. Starch cellulose is quite indigestible by the ptyalin or amylopsin, and it is only with difficulty permeated by these enzymes, so that digestion of uncooked starch grains is very much retarded. Moist heat has the effect of swelling the granulose and bursting the starch-cellulose envelopes, thus liberating the pure starch, which makes an opalescent paste if the water is sufficient in quantity. In any case it is made readily miscible with the saliva, and thus the action of the ptyalin is much facilitated.

2. **The Mastication of the Food.**—If the starchy food be bolted in unbroken pieces it is evident that, however thoroughly the food may be cooked, and however active and abundant the enzyme may be, the amylolytic action of the ptyalin must be slight, because not brought into proper physical relation to the starch.

A thorough mastication of the food breaks it up into minute pieces and mixes the saliva with it, so that the enzyme is brought into contact with a much larger proportion of starch than could be possible otherwise.

The time required for thorough mastication is another important element because the change in the starch may be well advanced before the food leaves the mouth.

3. **The Temperature of the Mixture.**—After the well-cooked food is thoroughly masticated there are other important conditions which must be fulfilled if the digestive changes are to be rapid and extensive. The *temperature* affects the operation of any enzyme. The *optimum temperature* is approximately that of the blood (37° to 40° C.). Outside of these limits the action is progressively slower the farther removed from the optimum. The action is wholly suspended at 0° C., but the enzyme is not destroyed. The action is wholly suspended at 65° to 70° C., and the enzyme is destroyed. Much has been said about the effect of cold drinks upon digestion. A large portion of what has been said cannot be verified by experiment. Experiment has demonstrated that if the contents of a beaker be

diluted with 10 volumes of water at 0° C. the action of the ptyalin will be much retarded, partly because of the dilution and partly because of the marked change of temperature. When cold water is taken with meals it is usually taken in moderate quantities, so that the dilution is not sufficient to retard the action of the enzyme. It is usually taken sufficiently slowly to be warmed to almost blood temperature before it reaches the stomach, so that a glass of cold water taken a little at a time during the progress of a meal cannot be said to effect any demonstrable retardation upon salivary digestion in the stomach.

4. **The Reaction of the Mixture.**—The saliva is faintly alkaline because of the Na_2CO_3 which it contains. It is not necessary, however, that the reaction of the mixture of food and saliva be alkaline. The ptyalin acts quite as well in a neutral as in a faintly alkaline medium. Even a weak acid reaction does not stop—though it retards—the action of the enzyme, provided the acid be an organic acid like lactic acid. When HCl is combined with a protein, as acid albumin or syntonin, it will cause an acid reaction, but when the reaction is only faintly acid the action of the ptyalin may proceed, though at a slower rate. *Free HCl* will, however, stop the action of the ptyalin and destroy it when it is present in even so small a proportion as 0.003 per cent.[1] The free use of sour pickles and acid drinks must retard the action of the ptyalin. In the light of what will follow (*e*) it is evident that these acid foods may be taken late in a meal with less effect upon salivary digestion than when taken early in a meal.

5. **The Time of Salivary Digestion.**—The food is retained in the mouth not more than one minute at the longest. In this time the change has only begun, even when all the conditions are most favorable. The hydrochloric acid of the gastric juice is not present in the stomach until the stimulating presence of food induces its secretion. After it begins to be secreted some minutes elapse before the quantity of combined acid is sufficient to essentially retard the salivary digestion. It is estimated that from one to two hours or even more may elapse before salivary digestion is wholly suspended by the accumulation of *free* HCl.

The following conditions favor a prolongation of the time of salivary digestion: (I) The retardation of the secretion of hydrochloric acid. Nothing so quickly brings about a secretion of this acid as a glass of cold water. It is evident, then, that the drinking of water at the beginning of a meal will tend to shorten the period of salivary digestion. (II) The retardation of the permeation of the food by the acid. If the food is semisolid the acid permeates it slowly; if it is fluid the acid becomes readily mixed by diffusion as well as by movements of the stomach.

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[1] Chittenden, in Studies from the Laboratory of Physiologic Chemistry, Yale, 1904, vol. I.

Soups and drinks bring the contents of the stomach into a soupy mass which is readily acidified as soon as the HCl begins to be secreted. In this case again fluids at the beginning of the meal are unfavorable to the prolongation of the time of salivary digestion.

It is doubtful if in the average case there is any advantage in thus prolonging salivary digestion. The amylopsin of the pancreatic juice is a more active amylolytic enzyme than is ptyalin, and it has all the time necessary for its action without encroaching upon the time of other digestive processes.

4. MASTICATION.

This process is a purely mechanical and physical one and is wholly a voluntary one. With this process are associated those gustatory sensations and perceptions which are so enjoyable to most of mankind. The movements of the jaws, cheeks, and tongue stimulate the flow of saliva and ensure the thorough mixing of that secretion with the food (*insalivation*). The insalivation of the food produces three effects: (I) to *digest with ptyalin* the starch of the food; (II) to *lubricate* with *mucus* the mass of food, thus preparing it for deglutition; (III) to *dissolve* with the *water* of the saliva the soluble portions of the food—salt, sugar, etc.

In the discussion of the factors which influence salivary digestion the importance of the division of the food into fine particles was mentioned. It is quite as important in digestion by the other digestive fluids that the food be triturated. The enzyme gets access only to the surface of the particles of food. If the same volume of food present twice the surface one would expect it to digest in one-half the time, and such is approximately the case. Eight 1 mm. cubes of coagulated egg albumen would contain the same amount of albumen as one 2 mm. cube. They would aggregate twice the surface, and the time of digestion would be approximately half as long in the case of the 1 mm. cubes as in the case of the 2 mm. cubes.

The structures involved in mastication may be classified as skeletal, muscular, and nervous.

a. The Skeletal Structures of Mastication.

These include the maxillary bones as representatives of the endoskeleton, and the teeth as representatives of the exoskeleton. The function of mastication is variously specialized in different orders of mammals. It reaches its highest development in herbivora—whose food is difficult to masticate and yet requires the finest trituration in order to be digestible. The teeth of herbivora are the most perfect dental organs in the animal kingdom. The incisors are cupped and the molars have alternating ridges of dentine and enamel, and are self-sharpening. The carnivorous animals bolt their food with little chewing. The teeth, which are well developed, are the great, prehensile canines and the trenchant molars, which are especially adapted for breaking the bones of the prey. The omnivorous animals, to which kind man belongs, possess edged *incisors;* meagre *canines,* scarcely prehensile in man, though distinctly so in the gorilla; and *molars* with rounded cusps, well adapted to crush, but not at all capable of cutting, the food. The movements of the jaws differ distinctly in the different orders of animals above mentioned. The chopping movement is peculiar to the carnivora; the herbivora give the mandible a wide lateral and anteroposterior excursion, while the omnivora possess all of these movements in a moderate degree.

b. The Muscles and Nerves of Mastication.

The muscles and nerves of mastication include:

(*α*) THE FLEXORS or levators of the mandible: (I) the *masseter,* (II) the *temporal,* and (III) the *internal pterygoids.* All of these are innervated through the inferior maxillary division of the fifth cranial nerve.

(*β*) THE EXTENSORS or depressors of the mandible: (I) the *digastric,* (II) the *mylohyoid,* and (III) the *geniohyoid.* (I) posterior belly innervated by the inferior maxillary division of the V, and posterior belly by the VII cranial; (II) innervated by the inferior maxillary division of the V, and (III) innervated by the hypoglossal.

(*γ*) THE LATERAL MOVEMENTS of the jaws are produced by the alternate action of the *external pterygoids:* Inferior maxillary division of the V.

(*δ*) PROTRUDERS OF THE MANDIBLE: The external pterygoids *acting together.*

(*ε*) RETRACTOR OF THE MANDIBLE: The posterior portion of the *temporal.*

(*ζ*) THE CHEEK AND LIP MUSCLES: *Buccinator* and *orbicularis oris,* innervated by the buccal branch of the facialis.

(*η*) THE LINGUAL MUSCLES innervated by the lingual branch of the inferior maxillary division of the Trigeminus and by the Hypoglossus.

c. The Process of Mastication.

The food is cut by the incisors and crushed between the molars. The cheeks and tongue assist in bringing the food between the molars. The movements of the masticatory apparatus tend to stimulate the flow of saliva; the presence of food, especially acid, sweet, or dry food, tends also to stimulate the secretion of saliva.

The movements of mastication mix the saliva thoroughly with the food. The gustatory apparatus is stimulated by all substances which are soluble in water, and the olfactory apparatus by all volatile substances. The sensations derived from these two sense organs make up the so-called "tastes" and "flavors" of the foods. The pleasure derived from eating consists: (I) in the satisfying of the hunger, (II) in the enjoyment of the tastes and flavors. Hunger seems to be nature's warning of need for nutriment. The pleasure of the taste and flavor, besides assisting the animal in the choice of food, repays the animal for a thorough mastication of it.

5. DEGLUTITION.

After the food is made ready for the stomach by mastication, it is gathered, by the tongue, into a bolus or rounded mass between the tongue and the hard palate, and passed back to the pharynx, whose walls by a convulsive reflex act pass it to the œsophagus, along which it is pressed, by a peristaltic wave, into the stomach. The whole process of *swallowing* as here briefly outlined is called *deglutition.* The length of time required to perform the act is not commensurate with its complexity. The process may be analyzed as consisting of a voluntary and an involuntary part.

a. The Voluntary Part of Deglutition.

This consists in (I) *the formation of the bolus* by the cheeks, palate, and tongue, and (II) in the *pressing of the bolus backward* through the isthmus of the fauces—*i. e.*, between the anterior pillars of the fauces, which are the ridges marking the location of the palatoglossal muscles. Once the bolus of solid food (or the "swallow" of liquid) passes this *Rubicon* there is no turning back, the muscles of the pharynx grasp it reflexly and hurry it forward by wholly involuntary processes. The muscles and nerves of this voluntary initiatory step of deglutition have been enumerated under mastication, in which function they are important factors.

b. The Involuntary Part of Deglutition.

This consists in the transit of the bolus through the pharynx, and in its passage along the œsophageal canal.

1. **Pharyngeal Deglutition.**—The transit of the food through the pharynx is attended with two dangers, namely, the danger of a falling of a portion into the larynx, and the danger of regurgitation of a portion into the posterior nares. Pharyngeal deglutition consists, then, of three acts: transportation of the food; guarding against a false passage into the larynx; guarding against a false passage into the posterior nares.

(*a*) **Transportation** of the food through the pharynx and into the œsophagus is, according to Kronecker and Metzger[1] accomplished in two phases, a *projection phase* and a *clearing-up phase*. When the bolus reaches the isthmus of the fauces the tongue is closely approximated to the palate, blocking the way to the front. A convulsive contraction of the mylohyoid muscles puts the bolus under pressure and *projects* it across the pharyngeal cavity; the way is cleared by the simultaneous contraction of the hyoglossi muscles, which move the root of the tongue backward and downward. This movement depresses the epiglottis over the opening of the larynx, thus guarding that passage. In the case of liquid or semisolid food the entire transit of both pharynx and œsophagus is made in 0.1 second. The force of gravitation assists in this preliminary act—*the projection of the bolus. The clearing-up phase of* pharyngeal deglutition consists in a general peristaltic constriction passing from above downward and beginning 0.3 second after the constriction of the mylohyoids.

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[1] Arch. f. Physiologie, 1883, S. 328.

The first step in this phase consists of a contraction of the longitudinal muscles of the pharynx, which serves to pull the walls of the pharynx toward the bolus of food. The second step follows the guarding of the respiratory openings.

(*b*) **The Guarding of the Posterior Nares** is ensured by the elevation of the soft palate through the contraction of the levator palati and tensor palati muscles, by the contraction of the palatopharyngei muscles, and by the elevation of the uvula through the azygos uvulæ muscle.

(*c*) **The Guarding of the Laryngeal Opening** is ensured in part by the depression of the root of the tongue through the hyoglossi muscles as described above. Supplementing this and following it in time is the closure of the laryngeal opening by the epiglottis and the adduction of the vocal cords. (For muscles and nerves see Larynx.)

The second step in the clearing-up phase of food transportation through the pharynx consists of a peristaltic action of the constrictors of the pharynx. By this last act of pharyngeal deglutition any particles of food and any accumulated mucus are cleared from the pharynx and started along the œsophagus.

The two phases of deglutition above described (projection and clearing-up) seem to play parts of different relative importance according to the physical condition of different foods. In the case of liquid or very soft food the projection phase is the more important.

In drinking the cycle of swallowing acts follow in such rapid succession that there is not time for one to be completed before another is induced. Through the influence of the central nervous system all that portion of one deglutition, incompleted when a second deglutition supervenes, is suspended or inhibited.

Kronecker and Meltzer found that about 1.2 seconds elapse between the beginning of the contraction of the mylohyoid and the beginning of the contraction of the upper segment of the œsophagus.

There would be five complete pharyngeal acts in six seconds; this is just about the usual rate of deglutition when drinking. The œsophageal peristaltic waves must then be suspended during the progress of drinking. The observers cited found, furthermore, that the constrictors of the pharynx, though they would have time to contract, actually remain at rest; the deglutition being in this case a series of projections followed at the end by a clearing-up contraction of pharynx and œsophagus.

In the case of solid food in a well-formed bolus of considerable consistency the clearing-up phase always follows the projection of the bolus across the pharyngeal cavity.

2. **Œsophageal Deglutition.**—The bolus is passed along the œsophagus by a peristalsis which differs from peristalsis of the lower segments of the alimentary canal in being more under the immediate control of the central nervous system, as evidenced by the fact that removal of a segment of the œsophagus does not block the progress of the peristalsis, while the severing of a nerve suspends the peristalsis in the segment supplied by the severed nerve.

c. The Influence of the Nervous System upon Deglutition.

(*α*) THE CENTRE for involuntary pharyngeal and œsophageal deglutition lies in the upper end of the medulla, anterior to the respiratory centre. The boundaries of the centre have not been clearly defined.

(*β*) THE AFFERENT OR SENSORY IMPULSES which precipitate the act of involuntary deglutition reach the centre through the pharyngeal and the superior laryngeal branches of the *vagus*, and the palatal branches of the superior maxillary divisions of the *trigeminus*. The contact of the bolus of food with the mucous membrane supplied by the above-named nerves is a sufficient stimulus normally.

(*γ*) THE EFFERENT OR MOTOR IMPULSES which put the muscles of deglutition into activity are: the *hypoglossal* to the tongue and to the muscles which raise the larynx; the *glossopharyngeal, vagus, facial,* and *trigeminus* to the palate, fauces, and pharynx; and the *vagus* to the larynx and œsophagus.

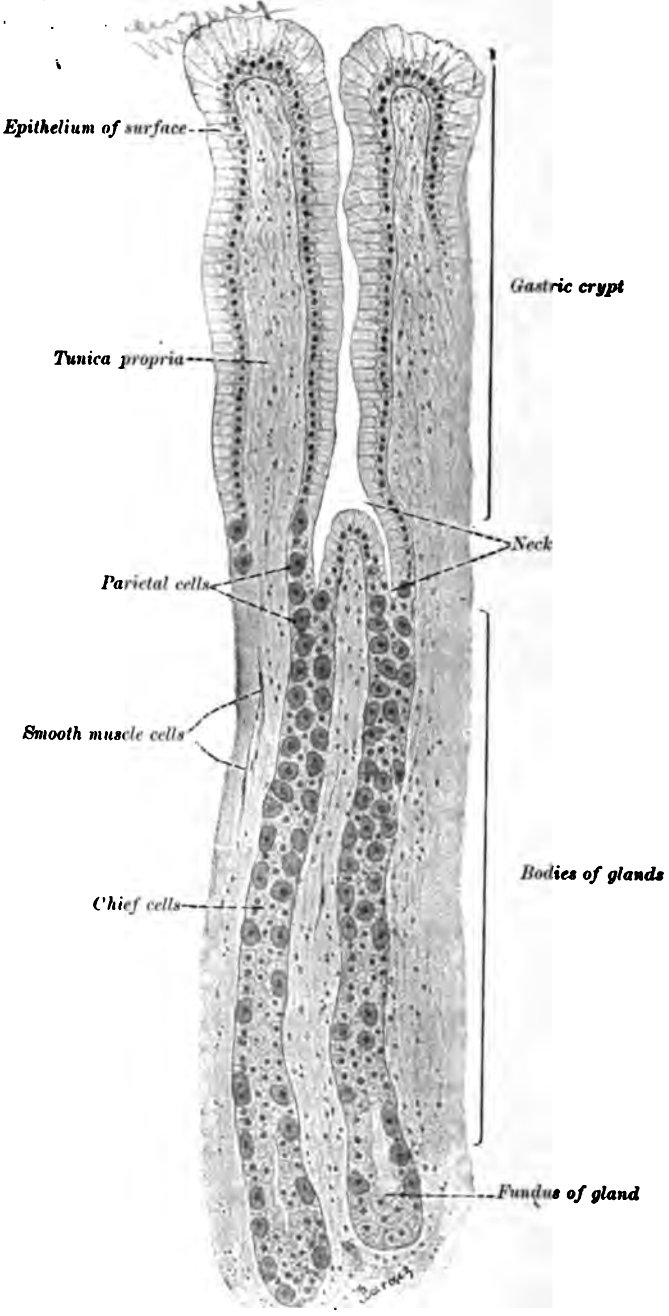
B. GASTRIC DIGESTION.

1. THE GASTRIC JUICE.

a. The Secretion of Gastric Juice.

1. **The Structure of the Gastric Glands.**—The general features of the secretion of gastric juice are the same as those of the secretion of saliva. The differences are specific rather than generic and are incident to the location and the specialized function.

Fig. 172



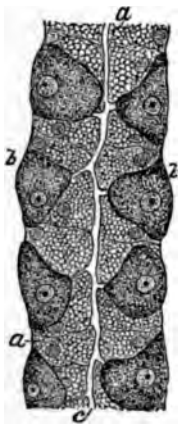
From a section through the human gastric mucous membrane in the region of the fundus. (Szymonowicz.)

The gastric glands are usually classified as cardiac and pyloric, because the glands of these two regions differ both functionally and structurally. The cardiac glands (see Fig. 172) possess two kinds of active cells, the "*chief*" or *central cells* and the *parietal cells*.

The columnar central cells are filled with a fine reticulum, and possess an amount of granular matter varying with the phase of activity. The discoidal or crescentic parietal cells do not lie beside the main lumen of the gland, but each cell possesses a diverticulum from the main lumen. (See Fig. 173.)

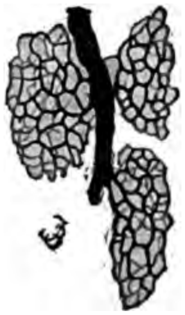
Besides the diverticula shown in Fig. 173 there are minute capillary branches of each diverticulum, which surround the parietal cells. (See Fig. 174.)

FIG. 173



Portion of cardiac gland of dog, highly magnified: *a, a,* the central or chief cells next the lumen (*c*); *b, b,* the parietal or acid cells connected with the lumen of the tube by short lateral branches which extend to the cells. (Piersol.)

FIG. 174



From fundus gland of a mouse. Basket-shaped plexuses of capillaries are seen to surround three oxyntic (acid-secreting) cells and to open into the gland lumen. (Szymonowicz.)

There has been some controversy about the function of these cells. The following facts deserve consideration in this connection: (I) The cells vary in size during different phases of glandular activity, being larger at the beginning than at the end of secretion. (II) Each cell is provided with a special system of little ducts or lumena. (III) The parietal cells are the only cells peculiar to the cardiac end of the stomach. (IV) The secretion from the cardiac end of the stomach contains hydrochloric acid, while the secretion from the pyloric end of the stomach contains no hydrochloric acid. This was demonstrated by Heidenhain, who separated the two portions of the stomach, giving each in turn an external fistulous opening. From the cardiac end of the stomach only was the secretion acid in reaction.

These facts seem to justify the following inferences: (I) The parietal cells are directly associated in the function of secretion of gastric juice. (II) They secrete a liquid that must find its way into the main lumen of the gland. (III) They secrete a liquid peculiar to the secretion of the cardiac end of the stomach. (IV) Hydrochloric acid being the only liquid peculiar to the cardiac end of the stomach, *the parietal cells must, therefore, secrete hydrochloric acid.* This course of reasoning is sufficiently convincing to satisfy physiologists of the certainty that in the parietal cells we see the site of the formation of hydrochloric, but it is reasoning by exclusion and cannot be accepted as an absolute demonstration.

The central cells are common to the cardiac and the pyloric glands. The secretion of pepsin is a function common to the cardiac and pyloric ends of the stomach. The central cells of these glands are larger at the beginning than at the end of secretion. They contain many granules at the beginning of secretion and few at the end of that process. There can be little doubt that the pepsin of the gastric juice is formed in the central or chief cells of the cardiac and pyloric glands.

The pyloric glands differ from the cardiac glands, first in general form—the ducts of pyloric glands being long and relatively wide. Into this duct empty several more or less tortuous tubules. (See Fig. 175.)

2. **The Secretion of Pepsin.**—This is one of the essential constituents of the gastric juice and its formation within the cells corresponds closely to the formation of the ptyalin in the cells of the salivary glands. The granules formed in the cells during the period of rest represent a mother-substance of pepsin or a zymogen which has been called *pepsinogen.* During the secretion of gastric juice the zymogen is subjected to a further metabolism which changes it to pepsin. The pepsin-secreting power of the pyloric glands is much below that of the cardiac glands. It is contended by some[1] that any pepsin found in the pyloric segment of the stomach, or extracted from the mucous membrane of that segment, was secreted by the cardiac glands and simply absorbed by the pyloric mucous membrane, or taken up by "*infiltration.*" Heidenhain's investigations have, however, demonstrated conclusively that *pepsin is secreted by the pyloric glands.*

Much that has been said regarding the secretion of pepsin is equally true for the milk-curdling enzyme, *rennin.* Rennin is secreted by the central or chief cells of the cardiac and pyloric glands. It is secreted more abundantly by the cardiac than by the pyloric glands. It exists in the gland cells in a granular zymogen (renninogen) which may be extracted as such and then changed to the active form, rennin. In fact, the first zymogen found was that of rennin. The granules of pepsinogen and renninogen exist together in the gland cells and it is impossible to differentiate them morphologically.

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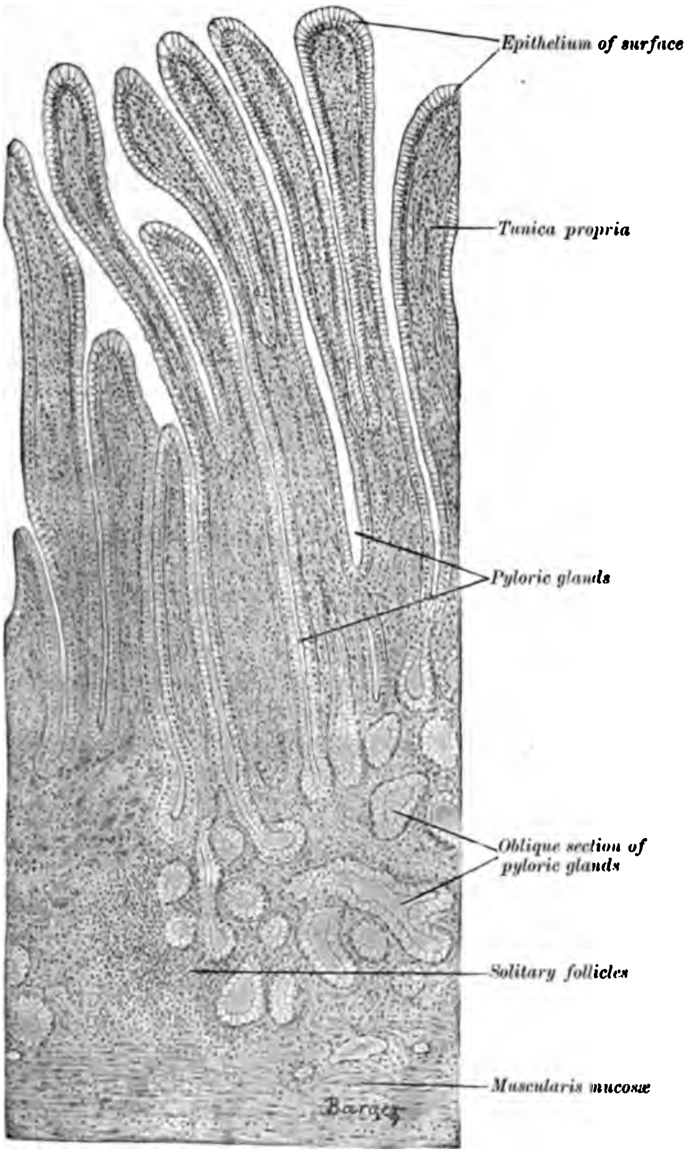
[1] Wassmann. "De digestione monnula," Berolini, 1839; von Wittich, "Ueber die Pepsin wirkung der Pylorus drüsen," Arch. f. d. ges. Physiologie, Bonn, 1878.

FIG. 175



From a section through the human gastric mucous membrane in the pyloric region. (Szymonowicz.)

Recent work by Pawlow and Pazaschtschuk, Lawrow, and Salaskin seems to demonstrate that these ferments (pepsin and rennin) are simply different manifestations of the same ferment.[1]

3. **The Secretion of Hydrochloric Acid.**—Hydrochloric acid is without doubt secreted by the parietal cells of the cardiac glands. From what materials and by what process the acid is formed is an undecided question.

"There is little doubt that the material for the formation of the HCl is the sodium chloride, which forms a large part of the ash of blood and lymph. The plasma and lymph is alkaline through presence of sodium carbonate. How can chlorine be liberated from the sodium chloride of the alkaline plasma? Only two methods are possible: 1st, either the Cl must be separated from Na through some active energy, as electricity—in electrolysis—or, 2d, the Cl must be displaced by another acid. There is no ground for believing that the separation is effected by electricity." (Bunge, *Physiological Chemistry.*) But it is generally believed that only a stronger acid can displace a weaker one. In 1871 Julius Thomsen demonstrated that "every acid can displace, from its combination with any base, a part of any other acid."[2] This ability is not through affinity alone, but through another characteristic which Thomsen called "*avidity.*" When equal parts of HCl and acetic acid act together upon Na_2CO_3 in aqueous solution only $\frac{1}{34}$ of the Na will combine with the acetic acid; so the latter acid has only $\frac{1}{34}$ the *avidity* of HCl. But if the proportion of acetic acid be increased, more than $\frac{1}{34}$ of the Na will combine as sodium acetate; and the more, the greater the preponderance of acetic acid.

This displacement of stronger acid by a weaker one when the latter is increased in proportion is called the "mass effect" of weak acids. "Even CO_2 (or H_2CO_3), one of the weakest acids, must be able through mass effect to displace a small part of any other acid." (Bunge.) The reaction might be written thus:

$$2NaCl + 1000H_2CO_3 = 999H_2CO_3 + 2HCl + Na_2CO_3.$$

Maly also suggested the following reactions as showing the possible source of the HCl:

$$\text{(I)}\ NaH_2PO_4 + NaCl = Na_2HPO_4 + HCl.$$

$$\text{(II)}\ 2Na_2HPO_4 + 3CaCl_2 = Ca_3(PO_4)_2 + 4NaCl + 2HCl.$$

That any of these reactions occurs has not been demonstrated. Most physiologists believe that the chlorine is liberated chemically in some way from one of the chlorides of the blood. But as Bunge says: "There is less obscurity in the liberation of free HCl than in the ability of the parietal cells to secrete the HCl toward the lumen of the gland and discharge the other products toward the blood." In other words, even after we have accounted, chemically, for the formation of the hydrochloric acid we will still have to fall back upon the vital activity of the cell to account for its ability to select from the blood the compounds needed in the reaction, and to return to the blood a part of the products of the reaction while another part is secreted into the lumen of the gland.

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[1] See Zeitsch. f. physiol. Chem., vol. xxxvi. p. 290.

[2] J. Thomsen, "Thermo-chemische Untersuchungen," Poggendorff Ann., 1871, 143.

b. Factors which Control Secretion of Gastric Juice.

1. **The Innervation of the Stomach.** (*a*) **Anatomically.**—(I) The left vagus is distributed to the lesser curvature and anterior surface of the stomach, besides sending communicating branches to the hepatic plexus. The right vagus passes behind the viscus, innervates the fundus and posterior surface, and sends communicating branches to the cœliac, splenic, and renal plexuses. (II) Through these communicating branches the stomach receives sympathetic fibres from the splanchnics. (III) The gangliated plexus of Auerbach lies between the muscular coats of the stomach and the gangliated plexus of Meissner lies in the submucosa. (IV) The special plexuses of Openchowski, which innervate the cardia and pylorus.

Note that the innervation is cranial and sympathetic; thus far it is like the innervation of the salivary glands. Note, further, that there are present in the stomach at least two distinct diffuse gangliated plexuses.

(*b*) **Physiologically,** the innervation of the stomach may, in the light of recent work in the Pawlow Institute (St. Petersburg), be thus briefly summarized:

(*α*) EFFERENT FIBRES reach the glands of the stomach from the central nervous system through the *vagus* and through the *sympathetic system* (splanchnics). These two general sources supply the glands with: (I) vagus secretory, (II) vagus inhibitory, (III) sympathetic secretory, (IV) sympathetic vasoconstrictor, and (V) sympathetic vasodilator.

(*β*) AFFERENT FIBRES reach the central nervous system from the mucous membrane of the stomach through the vagus. But the secretory activity of the stomach is governed not alone by gastric stimuli. Not less potent than these are gustatory and olfactory stimuli impulses, which are received at the gastric secretory centre along the respective cranial nerves. Furthermore, the centre is influenced by the sight and even the thought of food; thus to the afferent paths we must add the optic nerve and association fibres from the cerebrum to the centre.

(*γ*) THE CENTRE FOR GASTRIC SECRETION exists as surely as did Uranus before Herschel discovered it; otherwise what is the significance of all these afferent and efferent paths? Until it is more definitely located we may safely assume that it is in the medulla oblongata, not far from other centres that preside over vital functions.

2. **The Response of the Gastric Glands to Stimuli.**—Much has been accomplished in the field by Heidenhain and others. It remained for Professor Pawlow and his pupils of the Institute of Experimental Medicine in St. Petersburg, to rework the whole subject and to illuminate it with many brilliant discoveries. No adequate presentation of this important subject can be made without rehearsing, in outline at least, the methods and the results of Professor Pawlow's decade of research.[1]

(*a*) **The Method.**—Dogs were used as subjects. They were subjected to the following operative procedures:

(*α*) ŒSOPHAGOTOMY, in which the œsophagus was divided and a double fistula made in the throat, enabling the experimenter to feed the animal by mouth, the food dropping out of the upper fistula (*sham feeding*), or to feed by introduction of food into lower fistula (*true feeding*). *Psychic feeding* was accomplished by passing food before the eyes and nose of the animal without permitting him to actually take it into his mouth.

(*β*) GASTROTOMY, in which the stomach was divided along the line *A B* (see Fig. 176) and sutured so as to form a "Pawlow pouch," possessing all the coats of the viscus, a fistulous opening upon the surface, and its full normal innervation, but no open connection with the main cavity of the stomach. (See Fig. 177.) [Pawlow, p. 12, 13.]

(*γ*) GASTRIC FISTULA, in which a fistulous opening is made into the main cavity of the stomach, with or without the pouch.

In some of the more complex experiments animals were subjected to all of these operations and lived for months comfortably.

(*b*) **The Results of the Researches** only can be given in this brief text.

I. "By a careful preparation of the vagus nerves, some branches were discovered whose excitation causes a secretion without any latent period, almost as promptly as the chorda tympani expels saliva. From the latter fact we must conclude that in the branches mentioned the secretory fibres of the pancreas have been anatomically separated from the inhibitory, and that the purely secretory nerves, on artificial stimulation, call into play the activity of the organ without any latent period. Finally, Dr. Popielski succeeded also in isolating branches of the vagus, which only inhibited and never called forth a secretion. If such inhibitory nerves exist, it is easy to understand their reflex excitation, both under normal conditions as well as during operations. Nor is the possibility excluded that reflex inhibition extends also to the secretory centres for the pancreas" [p. 61].

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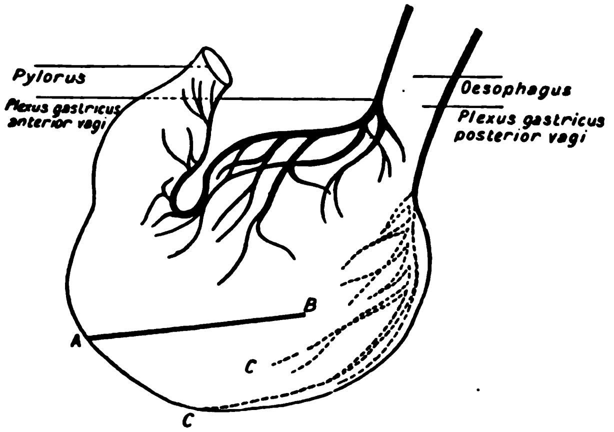
[1] For the source of this summary see the Work of the Digestive Glands. Lectures by Pawlow, translated by W. H. Thompson, M.D., of Dublin. Published by Charles Griffin & Co., London, 1902. References to this volume will be given by page in brackets.

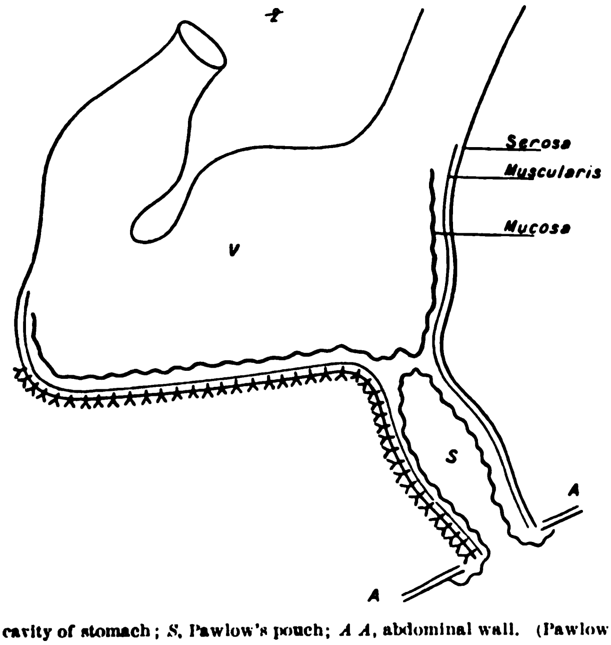
II. "We cannot doubt that secretory fibres for the stomach are present not only in the vagus, but also in the sympathetic" [p. 61].

FIG. 176


Pylorus
Plexus gastricus anterior vagi
Oesophagus
Plexus gastricus posterior vagi
B
A
C
C

A B, line of incision; *C*, flap for forming stomach pouch of Pawlow. (Pawlow.)

FIG. 177



V, cavity of stomach; *S*, Pawlow's pouch; *A A*, abdominal wall. (Pawlow.)

III. "It need hardly be said that, in addition to these special nerves, vasomotor nerves—constrictor and dilator—also pertain to the glands" [p. 61].

IV. "Just as men and animals in the world are only able to maintain their existence and constantly adapt themselves to changing circumstances by aid of the peripheral endings of their sensory nerves, so every organ, indeed, every cell of every organ, can only maintain its place in the animal microcosm, and adapt itself to the activity of innumerable associates, as well as to the general life of the whole, by virtue of the fact that the peripheral end apparatus of its centripetal nerves possess a specific excitability" [p. 64].

We must be prepared, therefore, to find that the stomach responds to special and not general stimuli, as has been for a long time assumed. Further, that its secretion is adapted in time of appearance, in quantity, and in quality, to the work which it has to accomplish.

V. "Every individual kind of food calls forth a particular activity of the digestive glands, with special properties of the digestive juices" [p. 82].

Pawlow's experiments on the stomach secretion consist in observations on the quantity and the character of the secretion with (I) *psychic feeding*, (II) *sham feeding*, and (III) *true feeding*, each kind of feeding being tested with the *typical foodstuffs*—egg albumen, starch paste, and fat, either liquid or solid—and with such *typical foods* as lean meat, bread and milk, taken separately or in combination.

VI. "Repeated attempts were made to excite a secretion of gastric juice by mechanical and chemical stimulation of the buccal mucous membrane. All such attempts failed" [p. 71].

VII. "When we call to mind the failure of our attempts to obtain a secretion of gastric juice by any stimulation whatever of the buccal mucous membrane, and at the same time see how constant and intense the action of this psychic impression is, we are forced to the inevitable conclusion that in our sham-feeding experiment the whole secretory effect is due to the psychic stimulus, that is to say, to the keen desire on the part of the animal for food and the satisfaction of enjoying it" [p. 73].

"We are therefore justified in saying that the *appetite* is the first and mightiest exciter of the secretory nerves of the stomach, a factor which embodies in itself a something capable of impelling the empty stomach of a dog in the sham-feeding experiment to secrete large quantities of the strongest juice. A good appetite in eating is equivalent from the outset to a vigorous secretion of the strongest juice; where there is no appetite this juice is altogether absent. To restore appetite to a man means to secure him a large stock of gastric juice wherewith to begin the digestion of the meal" [p. 75].

VIII. "As you see, the curve which represents the results of the direct introduction of flesh into the stomach ascends much more slowly, and does not attain anything like the height of that caused by normal feeding with the same food. But if the quantities obtained by direct introduction of the flesh be added to those of sham feeding, the resulting curve is almost identical with the normal" [p. 82].

We find, therefore, that feeding acts in two ways: first, as a pure *psychic stimulus*, appealing to the animal through gustatory, olfactory, visual, and other sensations, exciting a mental state (appetite) which in turn induces a copious secretion of gastric juice; second, the food acts directly upon the mucous membrane as a chemical stimulus, thus exciting a secretion adapted to the particular foodstuff.

As set forth in the last quotation (VIII) the total secretion in normal feeding is the sum of that induced by psychic stimulus plus that induced by chemical stimulus. The first is properly called "*appetite juice*," the second "*food juice*." Both of these components vary according to the kind of food ingested.

"*Mechanical stimulation* of the gastric mucous membrane—*i. e.*, presence of food, without reference to the chemical nature—does not cause any secretory response" [p. 86].

The gastric juice secreted in response to these various stimuli varies, (I) as to quantity, (II) as to degree of acidity, and (III) as to proportion of pepsin.

IX. "The juice, as it is poured out of the glands, always possesses the same *degree of acidity*. We do not, however, receive the juice directly from the glands, even in our method. After it is secreted by these it has to flow down over the alkaline mucous membrane and inevitably becomes partially neutralized—that is to say, has its acidity reduced."

"It is a rule, almost without exception, that the acidity of the juice is closely dependent upon the rate of secretion; the more rapid the latter, the more acid the juice, and *vice versa*" [p. 30].

"If the stomach has been washed several times in succession, not infrequently all connection between the rate of secretion and degree of acidity can be removed. Moreover, a short time ago we made observations in the laboratory upon a dog suffering from strongly marked hyperacidity of pathologic origin, but in no single sample of the juice did the acidity prove to exceed the normal. If all this be correct, the varying necessity for acid during the course of digestion is supplied by variations in the quantity of juice and not by changes in its acidity" [p. 31].

X. "*The foodstuffs* were tested with the following positive results: *Water, milk, gelatin*, and *meat extract* act as chemical stimuli of gastric secretion, the strongest being the meat extract. Water in quantities of ¼ to ½ litre must be accepted as a chemical excitant of gastric secretion, if only a weak one" [p. 98].

"In addition to water, we have at present found only one other chemical excitant—viz., in the extractive materials of flesh. Milk and solution of gelatin were, however, also found to be direct chemical stimuli to gastric secretion. The individual extractives such as kreatin, kreatinin—etc., were found to be ineffective" [p. 97].

XI. "Without any stimulating effect, but with a mild inhibitory effect, are starch and sugars. The remaining foodstuffs, such as fat and starch, proved in Dr. Chigin's hands not to have any exciting effects. Starch, whether boiled or unboiled, and mixed in different proportions with water, had no greater effect, but rather less than water alone. The same applies to grape-sugar and cane-sugar" [p. 97].

XII. "A new and very striking fact is here before us. Fat depresses —that is, inhibits—the normal energy of the secretory process" [p. 104].

XIII. *The foods* were tested, with the following results: "The greatest digestive power belongs to the juice poured out on bread, which for shortness we may name 'bread juice.' Its mean proteolytic power, according to Dr. Chigin, is represented by 6.64 mm. A diet of flesh calls forth a juice of 3.99 mm. digestive power, and one of milk of 3.26 mm. If we now turn to a comparison of these juices with one another we find, according to the law of Schutz and Borrisow, that 'bread juice' is represented by 44 (6.64^2), 'flesh juice' by 16 (3.99^2), and 'milk juice' by 11 (3.26^2)" [p. 33].

"Take, for example, the quantities of ferment which the stomach pours out on corresponding nitrogen equivalents of the various kinds of food: on bread, 1600 ferment units; on flesh, 430, and on milk, 340" [p. 36].

"These indicate that, on protein in the form of bread, five times more pepsin is poured out than on the same quantity of protein in the form of milk, and that flesh nitrogen requires 25 per cent. more pepsin than that of milk" [p. 37].

XIV. "*The digestion* requires both *appetite juice* and *food juice*. In the case of flesh this appetite juice affords important assistance to the 'food juice,' thereby determining a rapid digestion and shortening the stay of the raw product in the digestive canal. With other foods, for example, with bread, appetite juice is an indispensable condition to their digestion. If bread or egg albumen be eaten without appetite or introduced into the stomach unobserved, they lie there for a long time, just as stones lie, without the least appearance of digestion" [p. 101].

XV. "*Habituation* to one diet leads to an adjustment of the glands to that diet. If a dog has been fed for weeks on nothing but milk and bread, and is then brought to an exclusively flesh diet, which contains more protein, but scarcely any carbohydrate, a continuous increase of the protein ferment in the juice is to be observed. The capability of digesting protein waxes from day to day, while, on the contrary, the amylolytic power of the juice is found to be continuously on the wane" [p. 41].

XVI. "Sleep does not exercise the least influence on the secretory work of the gastric glands" [p. 123].

c. Chemical Composition of the Gastric Juice.

The most reliable and complete analyses of gastric juice are those made by Carl Schmidt. The human gastric juice was collected from a healthy woman who had a permanent gastric fistula made necessary by a traumatic stricture of the œsophagus. The analysis of gastric juice from the carnivorous animal is the mean of ten determinations from a dog whose salivary ducts had been ligated.

CONSTITUENTS OF THE GASTRIC JUICE.	HUMAN.	DOG.
Water	99.440	97.306
Solids	0.560	2.694
Organic	0.319	1.713
Pepsin, mucin, etc.		
Inorganic	0.241	0.981
HCl [0.1 % to 0.2 %]	......	0.334
$NaCl$	0.146	0.250
KCl	0.055	0.112
$CaCl_2$	0.006	0.026
NH_4Cl	0.021	0.047
$Ca_3(PO_4)_2$	0.013	0.171
$Mg_3(PO_4)_2$		0.023
$Fe_2(PO_4)_2$		0.008

Note that the principal organic substance is the enzyme. Mucin is always a constituent of the secretion of a mucous membrane. Among the salts one notes the presence of chlorides and phosphates, but the absence of carbonates, which formed an important constituent of the saliva, causing its alkalinity. The acidity of the gastric juice is not always due to HCl, but frequently to lactic acid, which is the product of a lactic acid fermentation which takes place in the contents of the stomach.[1] Note that the gastric juice of the dog is much richer in both organic and inorganic constituents than is human gastric juice. The HCl in the gastric juice of the dog ranges from 0.3 per cent. to 0.5 per cent. That it should be stronger is to be expected first because the diet of the carnivorous animal is largely a proteid diet which must follow either an *acid pepsin* digestion or a *trypsin* digestion. The bones which carnivorous animals eat can only be digested by a strongly acid gastric juice.

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[1] The bacterium lactis and allied species are able to attack starch as well as milk-sugar, so that the presence of lactic acid is possible even when the subject has had no milk. The following reaction has been suggested (Simon):

$$\text{(I)}\ 2(C_6H_{10}O_5)_n + nH_2O = nC_{12}H_{22}O_{11},\ \text{lactose.}$$

$$\text{(II)}\ C_{12}H_{22}O_{11} + H_2O = 4C_3H_6O_3,\ \text{lactic acid.}$$

2. THE CHEMISTRY OF GASTRIC DIGESTION.

Experiment shows that the active agents of the gastric juice are the *enzyme* and the *acid*.

If a typical protein, such as coagulated egg albumen, be put into a *neutral* solution of pepsin it will not be dissolved.

If a protein be put into a 0.1 to 0.3 per cent. HCl solution it will be modified both physically and chemically—it will swell up and become clearer, some proteins actually passing into a clear solution. The chemical change, though not understood in detail, is recognized as a chemical association, or possibly a typical chemical combination of the HCl molecule with the protein molecule. Such a compound is called an *albuminate* and is classified as one of the *derived proteins*. This particular albuminate is called *acid albumin*, or *syntonin*. Acid albumin, or syntonin, is precipitated by neutralizing the solution. It can be redissolved by weak acid or be converted into *alkali albumin* by weak alkali.

It must be evident from the above that of the active agents the acid must act first upon the albumin and globulin classes of proteins. If one bring gastric juice—either secreted or artificial—into contact with a native protein under favorable conditions the proteins will be rapidly changed to syntonin. Upon this syntonin the pepsin acts, inducing a series of hydrolytic cleavages.

As in the hydrolytic cleavages which starch undergoes under the influence of ptyalin, so here the process represents several steps. Just how many steps there are between the acid albumin or syntonin and the final product, peptone, is still an open question. The mid-products between the albuminates and the peptones are called *proteoses* in general.[1]

Of the proteoses two steps have been demonstrated—viz., primary proteoses and secondary proteoses. The secondary proteoses are appropriately so-called because they not only follow the primary proteoses in time, but are derived from them. The primary proteoses exist in two chemically separable forms named by Neumeister[2] *protoalbumoses* (protoproteoses) and *heteroalbumoses* (heteroproteoses).

The deuteroalbumoses exist in forms which are not chemically separable, but which give rise to a series of peptones also inseparable chemically. A part of the peptone formed by peptic proteolysis undergoes, under the influence of trypsin, further change which results in the formation of tyrosin, leucin, and allied nitrogenous bodies. The other part of the peptone is not acted upon by trypsin.

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[1] The mid-products of the native albumins are called the *albumoses*; of the globulins, *globuloses*; of casein, *caseinoses*, etc., but these distinctions, if justified by our present chemical knowledge, are certainly not necessary at present. Let us, therefore, group all of the mid-products between the syntonins and the peptones as *proteoses*.

[2] Lehrbuch d. physiol. Chemie.

Attempts to account for the phenomena of proteid digestion have given rise to two hypotheses: (I) Kühne's hypothesis of *cleavage into two co-ordinate hemi-* and *anti*-molecules, the former breaking up under the influence of trypsin into amino-acids, while the latter is changed to peptone; and (II) Moore's hypothesis of *cleavage, from the proteid molecule* of *subordinate, amino-acid molecules.* The reader remembers that in salivary digestion the starch molecule is subjected to a series of hydrolytic cleavages, but that these cleavages are not *co-ordinate.* In each cleavage a *subordinate* molecule maltose is split off from the carbohydrate molecule until the whole carbohydrate molecule is finally broken up into maltose molecules. According to Moore's hypothesis: "The different proteins, especially the proteoses, differ so little in chemical composition that the difference in their nature is probably due to a difference in atomic grouping. . . . Some of these groups are much more susceptible of decomposition than others. . . . Those albumoses which yield much amino-acid contain in their molecules more groups which are decomposable by trypsin. . . . Those which yield much antipeptone contain less of these decomposable groups. . . . In all cases that substance which we call antipeptone is the *remainder* after all of those groups which are attackable by trypsin have been removed in the form of amino-acids." The process which Moore outlines is in harmony with the facts and is analogous to ptyalin digestion. Moore's hypothesis presents no hypothetical substances; it utilizes only substances separable by chemical methods from all other substances.

The facts of peptic proteolysis may be summarized in the following table:

SERIES I.	SERIES II	CHARACTERISTICS.
Native Proteid.	Native Proteid.	Responds to xanthoproteic test, to Millon's test. Is indiffusible.
Syntonin.	Syntonin.	Soluble in dilute acids, insoluble in water, indiffusible.
	Proto-proteose	Soluble in H_2O; precipitated by $MgSO_4$, NaCl or $(NH_4)_2SO_4$ in Sat. Sol. Diffusible
Primary Proteoses.	Hetero-proteose	Soluble in dilute NaCl solution, precipitated by Sat. Sol. NaCl or $MgSO_4$ and $(NH_4)_2SO_4$. Diffusible.
Secondary Proteoses.	Deutero-proteoses.	Soluble in water. Precipitated by $(NH_4)_2SO_4$. Diffusible.
Peptones.	Peptones.	Soluble in water, not precipitated by $(NH_4)_2SO_4$ Diffusible.

3. FACTORS WHICH INFLUENCE GASTRIC DIGESTION.

1. **The Preparation of Food.**—Inasmuch as gastric digestion is confined to proteins, it is now in order to determine the influence of cooking upon proteolysis. Proteins may be divided into two classes for the consideration of this subject:

(*α*) PROTEINS WHICH ARE COAGULATED BY HEAT.—This class includes the native albumins and globulins. As already mentioned under cooking, the application of high temperatures to any of this class of proteins decreases the ease with which it may be digested. In the preparation of eggs (uncompounded), of clear lean meat, of beef juice or blood (serum albumin and serum globulin) just as little heat should be applied as is possible to do and make a palatable dish.

(*β*) PROTEINS WHICH ARE NOT COAGULATED BY HEAT. ***Albuminoids.***—*Collagen* is the sole representative of this class which is important here. Collagen enters into the formation of all of the connective tissues of the animal body. In preparing most cuts of meat one has to deal with a large proportion of connective tissue. If properly prepared it is digestible and nourishing; if not so prepared it is almost indigestible itself, and its presence keeps the digestive juices from gaining proper access to the simple proteins, and thus prolongs very greatly the period of their digestion. When connective tissue is subjected to heat in the presence of moisture, the collagen becomes hydrated into gelatin. The meat is then easily masticated, the digestive juices readily penetrate it, and the gelatin itself is readily digested.

2. **The Mastication of Food.**—Under mastication the importance of this process was urged. It is not less important for gastric digestion than for salivary digestion.

3. **The Reaction of the Contents of the Stomach.**—From what appeared above it is evident that gastric digestion cannot proceed in an alkaline medium. The first step in the process being the formation of acid albumin, it is important to determine what acids may serve the purpose.

(*α*) THE KIND OF ACID NECESSARY.—The hydrochloric acid of the gastric juice is nature's acid. Under certain conditions lactic acid appears in moderate quantities. Any conditions which lead to a decrease in the hydrochloric acid favor the appearance of lactic acid, a fermentation product. In peptic proteolysis *lactic acid may take the place of hydrochloric acid.* Several organic acids are taken with the food: *acetic acid*, in vinegar; *malic acid*, in rhubarb, strawberries, apples, etc.; *citric acid*, in lemons and oranges, and *tartaric acid*, in grapes. Any of these acids may supplement, or even replace, the hydrochloric acid in gastric digestion.

(β) The Amount of Acid Necessary.—Experiment shows that though 0.3 per cent. is the strength of the hydrochloric acid in pure gastric juice, that is not the strength necessary for the formation of acid albumin. The foods taken into the stomach dilute the acid very much, so that it is hardly likely that the acid of the stomach during digestion represents more than 0.1 per cent. of the whole contents of the stomach. Digestion proceeds rapidly in HCl of that strength. Just how strong the other acids should be is not determined. It is not likely that they could be effective in less than 0.1 per cent. strength. Experiment has shown that 0.1 per cent. to 0.4 per cent. represent average favorable limits with some variation in the lower limit for different organic acids. The presence of moderate quantities of organic acids probably exerts relatively little effect upon digestion. The tendency of many to use these acids very freely, together with the influence which the presence of other acids has upon the secretion of hydrochloric acid, makes this question of importance to the clinician. If one were to drink a large quantity of lemonade at the beginning of a meal it is evident that the strong acid reaction of the stomach would greatly retard salivary digestion. On the other hand, a moderate amount of any acid drink or food toward the end of the meal serves a double purpose in gastric digestion: (I) to stimulate the activity of the gastric glands; (II) to assist the HCl in the digestion of proteins.

4. **The Influence of Temperature.**—What was said of the influence of temperature upon salivary digestion applies equally to gastric digestion.

5. **The Influence of Dilution.**—Much has been said and written against the drinking of cold water with meals, and especially at the beginning of meals. There is more misconception regarding water than any other food. Without entering into a discussion of the details of the question, and without citing the numerous and reliable authorities, the author will briefly state a few of the fundamental facts regarding the relation of water to nutrition: (I) Water is a prime necessity to the animal body. Lack of sufficient water is just as certain to lead to a derangement of the nutrition of the body as is lack of sufficient solid food. Most people use too little water; few people use too much water. (II) The free use of water does not tend directly to the accumulation of fat. The statement that it does so is a fallacy, which arises from these facts: The free use of water facilitates the processes of nutrition and economizes food by utilizing a greater proportion of it. Under such conditions any excess of food tends to be deposited as reserve material in the form of fat. The reasonable thing to do, if one wishes to decrease the tendency to accumulate fat, is not to induce a pathologic condition by the decrease of the water, but to *simply decrease the fat-forming material —i. e., decrease the carbohydrates and fats.* (III) Cold water stimulates

the free secretion of gastric juice. Cold water in moderate quantity at the beginning of a meal thus hastens the gastric digestion and makes more efficient the antiseptic action of the gastric juice. Recalling what was said regarding the relation of water and other diluents to salivary digestion, it is evident that several of the factors which hasten and facilitate gastric digestion at the same time retard or stop salivary digestion. We have to choose between these two alternatives. Which process is the more important to the system? The amylolytic enzyme of the pancreatic juice is much more active than is ptyalin. The conditions for digestion of starches are more favorable in the intestine than in the stomach.

By far the most important processes which take place in the stomach are: (I) the disinfection of the stomach contents by the hydrochloric acid; (II) the digestion of proteins. The prolonging of salivary digestion is of much less importance than either of these. The reasonable thing to do is to stimulate the secretion of gastric juice. *Water is a most efficient agent in the stimulation of the secretion of gastric juice.*

6. **The Influence of the Movements of the Stomach.**—The movements of the stomach facilitate gastric digestion (I) by mixing the gastric juice with the food, and (II) by removing those portions already digested.

We shall find that movements of the stomach (to be discussed later) are *wholly involuntary.* If they are to be controlled or modified in character it must be through the influence of reflexes. One may indirectly influence the rate of the heart by influencing the factors which control the heart. In the same way, to a smaller extent, perhaps, one may influence the movements of the stomach by influencing the factors which control the stomach musculature. Cannon,[1] after a series of observations on the influence of the emotions upon the movement of the stomach, thus summarizes his results: "The stomach movements are inhibited (actually stopped) whenever the cat shows signs of anxiety, rage, or distress." That strong emotions inhibit the movements of the human stomach and thus retard gastric digestion is beyond doubt.

4. THE MOVEMENTS OF THE STOMACH.

The most recent and most valuable contribution to our knowledge of the movements of the stomach has been made by Prof. Cannon, of Harvard. The *Roentgen rays* were utilized in producing a series of sketches of the stomach in action. To make the contents of the stomach opaque to the rays, subnitrate of bismuth was mixed with the food. A clear conception of the gastric movements and of the effect of these movements may be gotten by reproducing here some of Cannon's figures, and quoting his summary:

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[1] The Movements of the Stomach, American Journal of Physiology, vol. i. p. 359.

(*a*) "THE STOMACH CONSISTS of two physiologically distinct parts: the pyloric part and the fundus. Over the pyloric part, while food is present, constriction waves continually course toward the pylorus. The fundus is the active reservoir for the food and squeezes out its contents gradually into the pyloric part."

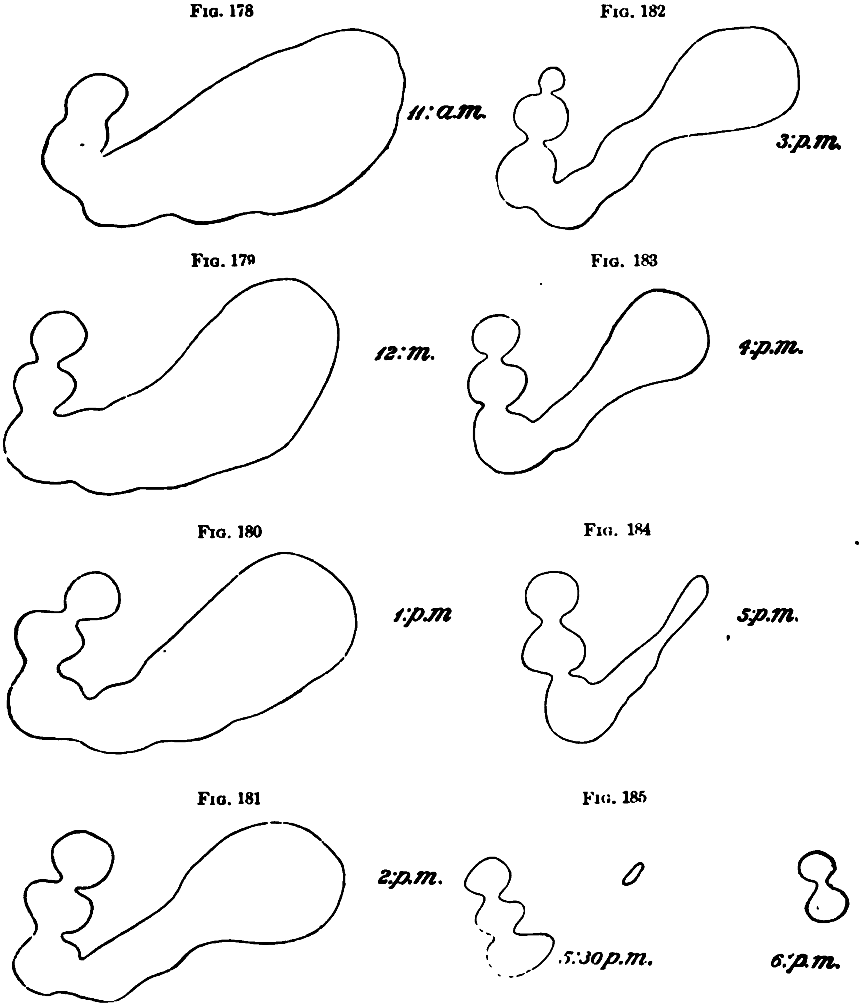


FIG. 178
FIG. 182
FIG. 179
FIG. 183
FIG. 180
FIG. 184
FIG. 181
FIG. 185

FIGS. 178 to 185. The movements of the stomach. These figures present the outlines of the shadow of the contents of the stomach cast on a fluorescent screen by the Roentgen ray. They show the change in the appearance of the stomach at intervals of one hour from the time of eating until the stomach is nearly empty. (Cannon.)

(β) "THE STOMACH IS EMPTIED by the formation of a tube between the fundus and the antrum, along which peristaltic constrictions pass. (See Fig. 158, p. 280.) The contents of the fundus are pressed into the tube, and the tube and antrum slowly cleared of food by the waves of constriction."

(γ) "THE FOOD IN THE PYLORIC PORTION is first pushed forward by the running wave, and then by pressure of the stomach wall is returned through the ring of constriction; thus the food is thoroughly mixed with gastric juice, and is forced by an oscillating progress to the pylorus." (See Fig. 178 *et seq.*)

(δ) "THE FOOD IN THE FUNDUS is not moved by peristalsis, and consequently it is not mixed with the gastric juice; salivary digestion can, therefore, be carried on in this region for a considerable period without being stopped by the acid gastric juice."

(ε) "THE PYLORUS DOES NOT OPEN at the approach of every wave, but only at irregular intervals. The arrival of a hard morsel causes the sphincter to open less frequently than normally, thus materially interfering with the passage of the already liquefied food."

(ζ) "SOLID FOOD REMAINS in the antrum to be rubbed by the constrictions until triturated, or to be softened by the gastric juice, or later it may be forced into the intestine in the solid state."

(η) "THE CONSTRICTION WAVES have, therefore, three functions: the *mixing*, *trituration*, and *expulsion* of food."

5. VOMITING.

a. The Mechanism of Vomiting.

In discussing this subject one must differentiate between (I) mild vomiting without nausea and (II) violent vomiting with nausea. Dogs and infants are likely to overload the stomach. The latter responds by a firm contraction of the pylorus or sphincter antri pylorici followed by a general contraction (a reversed peristalsis) of the walls of the stomach, the result being a regurgitation of a part of the just-swallowed food. That there is no nausea associated with this act is evidenced by the fact that the "dog returneth to his vomit," eating the food a second time; if the dog were nauseated he would not do that. But in adult man, the act of vomiting is generally preceded by a feeling of nausea, and usually there is a rush of saliva into the mouth, caused by a reflex stimulation through the afferent fibres of the gastric vagus and the efferent chorda tympani. After this a deep inspiration is taken and the glottis closed so that the diaphragm is firmly pressed down upon the abdominal contents; and it is kept contracted while a violent contraction of the abdominal muscles forcibly compresses the stomach, whose contents are ejected. This movement is so sudden that the sluggishly contracting involuntary muscles of the stomach walls do not have time to assist.

b. The Influence of the Nervous System upon Vomiting.

(*α*) THE EFFERENT IMPULSES pass to the pyloric sphincters, the diaphragm, the abdominal muscles, and the muscles of the larynx and pharynx through the vagus, phrenic, lower intercostals, and the superior maxillary division of the V.

(*β*) THE VOMITING CENTRE, though not definitely located, exists somewhere in the medulla. The muscles which are most active in vomiting are the respiratory muscles. The vomiting centre must be associated with the respiratory centre; it may be identical with the respiratory centre in whole or in part, or it may, under particular conditions, simply dominate the respiratory centre. The vomiting centre, indefinite though it is anatomically, is definitely influenced by certain afferent impulses.

(*γ*) THE AFFERENT IMPULSES reach the medullar centre through: (I) the vagus, which is stimulated by any gastric irritant; (II) the trigeminus and the glossopharyngeal, which are stimulated when the uvula and fauces are tickled; (III) the afferent nerves supplying the urogenital tract, stimulated by irritation of that tract—*e.g.*, uterine nerves stimulated during pregnancy; (IV) finally, impulses may reach the vomiting centre from the cerebrum or cerebellum which may induce vomiting. These impulses may be caused by certain pathologic conditions, or may be induced through the cerebrum by certain sights, odors, or tastes; or may be induced purely psychically through the memory of certain experiences which were associated with nausea. Disturbances of equilibrium may, through this same *central* influence, induce vomiting.

Drugs which induce vomiting are called emetics.

C. INTESTINAL DIGESTION.

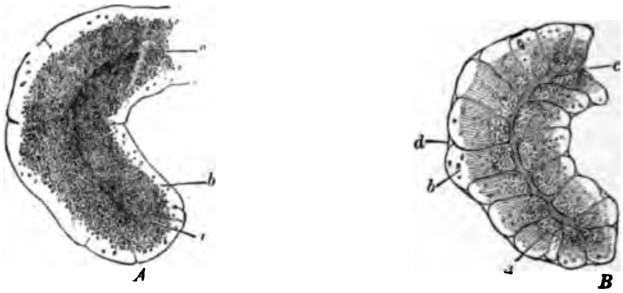
1. THE DIGESTIVE FLUIDS.

a. The Secretion of Pancreatic Juice.

The pancreas represents the compound tubular type of glands. The general arrangement of its ducts and tubular alveoli is shown in Fig. 164, under *Secretion*. The structural changes which take place in the cells of the pancreas during secretion are quite like those which are observed in the salivary glands during their activity, and these changes have the same significance. During the resting stage

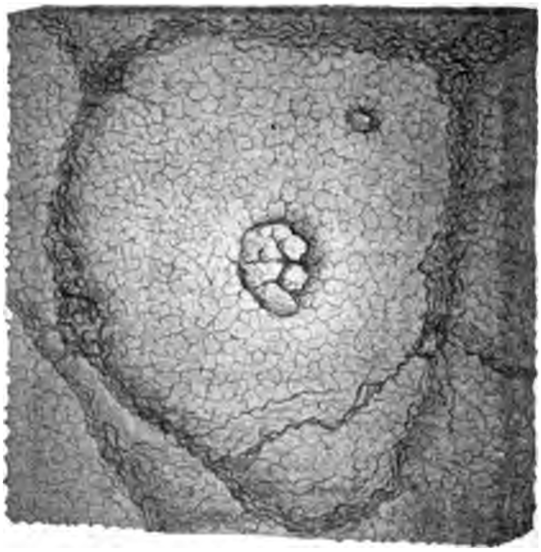
(Fig. 186) the cells become loaded with zymogen granules, and their outlines are less clearly seen. After a period of secretion the granules become much less numerous, striæ appear in the cytoplasm, and the unmodified cytoplasm is relatively much more abundant. The appearances justify the conclusion that parts of the secretion—the ferments—are formed from the granules; that these granules become

FIG. 186



Part of an alveolus of the rabbit's pancreas: *A*, at rest; *B*, after active secretion. *a*, the inner granular zone, which in *A* is larger and more closely studded with fine granules than in *B*, in which the granules are fewer and coarser; *b*, the outer transparent zone, small in *A*, larger in *B*, and in the latter marked with faint striæ; *c*, the lumen, very obvious in *B*, but indistinct in *A*; *d*, an indentation at the junction of the two cells, only seen in *B*. (From Schafer, after Foster and Kühne.)

FIG. 187



Framework of a lobule of the human pancreas, showing the connective tissue of an island of Langerhans. (Flint.)

exhausted during secretion, and are formed during rest at the expense of the cytoplasm. The cytoplasm, in turn, is replenished during the secretory activity of the gland, the cells apparently seizing the opportunity when the blood supply is abundant to secure the needed nutriment. During the resting period the granules are formed at the expense of the cytoplasm.

b. Factors which Control the Secretion of Pancreatic Juice.

The secretion of pancreatic juice varies with the phase of digestion, beginning soon after a meal and reaching a maximum (in the dog) from one to three hours after the meal, and gradually decreasing as digestion progresses. This relation of pancreatic secretion to conditions in the alimentary canal makes it certain that the secretion is a reflex act.

1. **Innervation of the Pancreatic Gland.**—This is given in general above. (See Fig. 160.) One may recall the double source, vagus and sympathetic, and that there are secretory fibres and vasomotor fibres. The afferent fibres pass to the centre along the vagus, not from the pancreas, but from the duodenum. This makes it possible for conditions in the duodenum to modify the activity of the gland.

2. **Conditions which Modify Activity of Pancreas.** (*a*) **Psychic Stimulus.**—As in the stomach, so in the pancreas, the psychic stimulus is normally the first to act.

I. *Psychic Influence.*—"In the experiment of teasing the animal by offering it food, the pancreatic flow also generally begins after two or three minutes. This appears to me to point to a direct psychic influence through the secretory nerves of the pancreas."[1]

(*b*) **Chemical Stimuli.** II. *Action of Acids.*—"During the acute experiment already described a solution of hydrochloric acid is poured into the duodenum. By this means a long-continued and vigorous secretion of pancreatic juice is called forth. If the vagus nerve be now strongly stimulated a slowing—often to complete standstill—of the secretion is obtained every time without exception. Excitation of the sympathetic, on the other hand, only slows the secretion, and this after the lapse of some time" [p. 60].

"No particular difference in the exciting effect of various acids was noticed. The acids investigated were phosphoric, citric, lactic, and acetic, in addition to the hydrochloric" [p. 114].

III. *Action of Water.*—"When water is poured into the stomach the result is a secretion of pancreatic juice."

"The conclusion is clear and free from objection, namely, that water is an independent and direct exciter of the nervous mechanism of the pancreas" [p. 125].

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[1] Pawlow. The Digestive Glands, p. 124.

IV. *Action of Organic Foods.*—"Dr. Dolinsky poured fluid oil into the stomach of dogs, and subsequently observed a more or less considerable flow of pancreatic juice."

"The experiment affords us adequate grounds for concluding that fat is an independent exciter of the pancreatic gland" [pp. 121, 122].

"When Dr. Walther fed a dog with bread, the pancreatic fluid possessed as much stronger amylolytic action than the juice obtained at a corresponding period, and with the same rate of flow after a meal of flesh" [p. 120].

(*c*). **Inhibition of Pancreatic Secretion.**—V. "An addition of sodium bicarbonate to the food for a length of time markedly depresses the secretory activity of the pancreas, which falls to an unusually low point" [p. 126].

"Sleep does not exercise the least influence on the secretory work of the pancreatic glands" [p. 123].

(*d*) **Summary.**—VI. "If we now sum up these facts, we are in a position to say that there are some excitants common to the gastric glands and to the pancreas. Among these probably the psychic effect, also water, and the strong craving for food and water, are to be included. But, in addition, both organs have their *specific stimuli;* for the gastric glands, the extractive substances of meat, and *for the pancreas, acids and fat*" [p. 125].

IX. "The acid gastric juice causes secretion of the pancreatic fluid by its acidity and in direct proportion to it; that is to say, while the acid constituent of the sodium chloride is taken up by the peptic glands and then passed on into the cavity of the stomach, the basic element, the sodium, serves for the preparation of pancreatic fluid. And thus the two constituents of the sodium chloride meet again in the alimentary canal and reproduce the salt. If the acid excites a flow of pancreatic juice, with the object, among others, of neutralizing itself, we should in consequence expect to meet with variations in the alkalinity of the juice, apart from the content of ferment, and determined by the acidity of the exciting fluid; and this is indeed the case; however, the juice is always produced for digestive purposes, and never merely for neutralization of acids" [p. 119].

X. "We see from the above an instructive instance of how the work of one segment of the alimentary canal is connected with and dependent upon that of the previous one. Thus, the saliva, which moistens everything dry, is able to act as an exciter of gastric secretion by virtue of its content of water. In the stomach itself it is in this way ensured that the psychic secretion which is the forerunner of digestion is continued by the influence of the saliva. The acid of the gastric juice acts in its turn as an excitant of the pancreatic gland, and thus the mutual influence which the digestive glands exert upon each other is clearly manifested" [p. 116].

c. The Composition of the Pancreatic Juice.

The sensitiveness of the pancreas to any operative procedures makes it difficult to get a normal secretion from a fistula. The Pawlow fistula is made by the insertion of a T-tube in the duct of the gland, so that at will the secretion may be drawn off or turned into the duodenum. The establishment of the fistula is followed by inflammatory changes. Before these changes occur a secretion may be caught which is called temporary. After the inflammatory changes have subsided the secretion approaches the normal qualitatively, though it contains a much smaller proportion of solids.

The following table gives two analyses by Carl Schmidt[1] from temporary and permanent fistulæ; also an analysis by Zawadsky[2] of normal human pancreatic juice:

CHEMICAL COMPOSITION OF PANCREATIC JUICE.

CONSTITUENTS.	FROM A TEMPORARY FISTULA (DOG).	FROM A PERMANENT FISTULA (DOG .	HUMAN PANC. JUICE.
WATER.	90.08	97.68	86.405
SOLIDS:	9.92	2.32	13.595
Organic: Enzymes, etc.	9.04	1.64	13.251
Inorganic.	0.88	0.68	0.344
Na_2CO_3	0.06	0.33	
NaCl	0.74	0.25	
KCl	trace.	0.09	
Ca, Mg and Na phosphates.	0.08	0.01	

The pancreatic juice contains several important constituents:

1. **Enzymes.**—(I) An amylolytic enzyme—*Amylopsin.* (II) A proteolytic enzyme—*Trypsin.* (III) A lipolytic enzyme—*Lipase.*
2. **Alkaline Salts.**—Na_2CO_3, and Na_3PO_4.

The influence of the salts is to make the alkalinity of the pancreatic juice equal to 0.2 to 0.4 per cent. of NaOH.

d. The Composition of the Succus Entericus.

This fluid is secreted by the crypts of Lieberkühn. The secretion is caught by making a fistula. The Vella-Thiry fistula is formed by cutting across the intestine at two places, 10 to 30 cm. apart, without interfering with the blood supply, restoring the continuity of the intestine, stitching both ends of the isolated piece to the abdominal wall, leaving a double fistulous opening. Fluid caught from such a fistula is limpid, opalescent, has a specific gravity ranging from 1.010 to 1.014, an alkalinity of nearly 0.5 per cent. NaOH; it contains proteins, and coagulates on standing. It contains 2 to 3 per cent. of solids, of which 0.7 per cent. to 0.9 per cent. is ash. Human succus entericus from the ileum near the ileocæcal valve[1] contained a much smaller proportion of solids, and had a specific gravity 1.0069.

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[1] Quoted by Maly in Hermann's Handbuch d. Physiol., Bd. v. (2), S. 189.

[2] Zentralbl. f. Physiol., 1891, Bd. v. S. 179.

The most important constituents of the succus entericus are: (*a*) Enzymes: *Enterokinase* and *Invertin.* (*b*) Alkaline salts: Na_2CO_3, etc.

As in the case of the gastric and pancreatic juices, so is the succus entericus secreted through the action of specific stimuli: (I) Indigestible substances like cellulose or connective tissue act as mechanical stimuli and cause a free secretion of water, the purpose evidently being to wash the indigestible matter along the intestines. (II) Pancreatic juice stimulates a free flow of succus entericus rich in *Enterokinase.*

e. Composition of the Bile.

The consideration of the bile in its relation to metabolism will be taken up later. It will be sufficient to summarize its composition here, and to discuss under digestion only those features which especially influence digestion.

TABLE SHOWING THE COMPOSITION OF HUMAN BILE.

CONSTITUENTS.	FROM GALL-BLADDER.	FROM FISTULA.
Water	89.81	98.72
Solids	10.19	1.28
Organic:		
Glycocholate of sodium	5.65	0.16
Taurocholate of sodium		0.06
Cholesterin, lecithin, fats, and soaps	3.09	0.04
Mucin, pigment, epithelium, etc.	1.45	0.15
Inorganic salts:		
Na_2CO_3, Na_2HPO_4	0.63	0.84

Note that the bile contains no ferment. Its most important constituents are the Na_2CO_3, the Na_2HPO_4, and the glycocholate and taurocholate of sodium. The daily quantity of bile secretion varies from 500 c.c. to 800 c.c.

2. THE CHEMISTRY OF INTESTINAL DIGESTION.

a. The Action of the Pancreatic Juice.

The pancreatic juice is active chemically through its alkaline salts and its enzymes. The alkaline salts of the intestinal fluids neutralize the acids which enter the duodenum from the stomach and, in the typical case, make the intestinal contents distinctly alkaline. In an alkaline medium all of the enzymes act more vigorously than in a neutral or faintly acid medium.

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[1] Tabby and Manning, Guy's Hospital Reports, London, 1891, vol. xlviii. p. 277.

1. **The Amylolytic Enzyme—Amylopsin.**—This enzyme is practically identical with ptyalin in all its properties except that its action is very much more rapid. Like ptyalin it acts best in an alkaline medium, and like that enzyme it changes starch to maltose. In the discussion of salivary digestion it cannot have escaped the attention of the reader that the ptyalin, under the most favorable circumstances, digests only a small proportion of the starch. Due to the imperfect cooking to which starchy foods are so frequently subjected, to the imperfect mastication and insalivation which are so prevalent, and to the almost universal dilution of the contents of the stomach with liquid foods or drinks, the action of the ptyalin is reduced to a most unimportant role. It is to the amylolytic enzyme of the pancreatic juice that we must look for the digestion of the amyloses.

The conditions under which this enzyme acts are most favorable; the temperature, the reaction, the degree of dilution, the trituration of the foods by the stomach are all favorable to rapid action of the amylopsin. Even raw starch is readily digested *in vitro* by the amylopsin. The conditions to which incompletely cooked starch is subjected in the stomach probably make it more easily digestible than is the raw starch used in laboratory experiments.

One may thus sum up the action of amylopsin: (I) It acts upon raw or cooked starch, causing a series of hydrolytic cleavages identical with those caused by ptyalin (which see). The hydrolysis is probably complete, resulting finally in producing *maltose, from starch.* (II) It acts upon the dextrins which have been previously formed by ptyalin—viz., amylodextrin, erythrodextrin and achroödextrin, completing the hydrolytic changes already begun; thus *producing maltose from dextrins.* (III) It acts upon *glycogen, changing it to maltose* through a series of cleavages parallel to or identical with those observed in the amylolytic digestion of starch.[1]

2. **The Proteolytic Enzyme—Trypsin.**—The protein-digesting enzyme of the pancreatic juice differs from that of the gastric juice in requiring an alkaline medium instead of an acid medium for its activity.

The first step of tryptic proteolysis is the formation of *alkali albumen.* This at once initiates a series of hydrolytic changes which, though parallel to the changes of peptic proteolysis, are not identical with them. The proteoses formed cannot be chemically separated into primary and secondary proteoses. There is, therefore, no proto-proteose and no heteroproteose. ***Deuteroproteoses*** **are present in several slightly varied forms, but all of them fulfilling the requirements of deuteroproteose or deuteroalbumose. The deuteroproteose formed in tryptic proteolysis is apparently identical in its response to chemical reactions with the deuteroproteose formed in peptic proteolysis. Neumeister finds that there are several deuteroproteoses formed in tryptic digestion, and that all of them yield on further cleavage both peptone and amino-acids.**

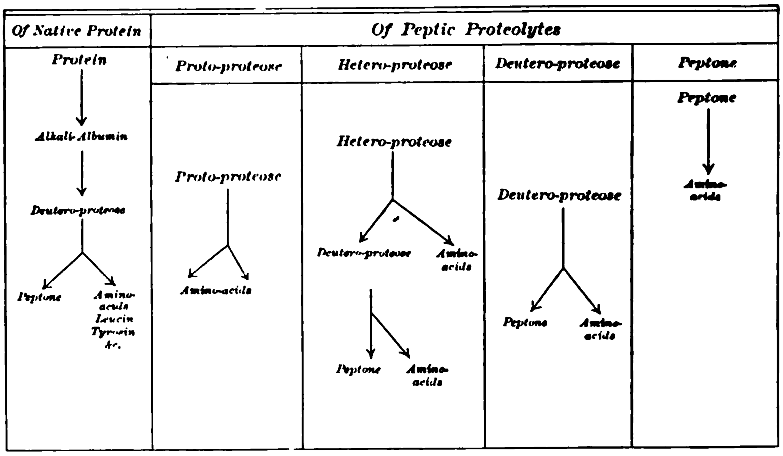
---

[1] The fact that the amylolytic ferment is absent from the pancreatic juice of infants makes it evident that they are not prepared by nature for starchy foods. Milk is nature's food for mammalian young, as witness all indications both in the mother and offspring. In the young mammal there are: (I) abundant and active milk-curdling enzymes; (II) proteolytic enzymes; (III) a fat-splitting enzyme, and (IV) an inverting enzyme.

The deuteroproteose of tryptic proteolysis gives rise to peptone and to the series of amino-acids—*i. e.*, there is experimental evidence of a *subordinate hydrolytic cleavage* of deuteroproteose but no experimental evidence of a *co-ordinate cleavage* into two peptones.

The action of trypsin upon native proteins and upon peptic proteolytes may be thus summarized:

Table of Tryptic Proteolysis.



The peptone of tryptic digestion is the form in which most of the protein foodstuffs are absorbed. **From this substance and from** some sulphur-containing compound, **protoplasm and other higher proteins** seem to be built up **by a process of anabolism. It is im**portant to determine the constitution of this substance. **There is** strong evidence that it is identical with Siegfried's ***Fleischsäure.***[1]

Both compounds react the same in **the biuret test; both fail to** respond to Millon's reagent; both are very **hygroscopic; both** yield, on decomposition with hydrochloric acid, **lysin and lysatinin. Fleisch**säure has been obtained directly **from the products of advanced** tryptic digestion. Both of the bodies **under consideration are easily** soluble in water. From a hot alcoholic solution Fleischsäure crystallizes in minute crystals. Siegfried has determined the formula of Fleischsäure to be $C_{10}H_{15}N_3O_5$ (mol. wt. 257), Sjöquist[2] determined the molecular weight of peptone (cryoscopic method) to be 250. In the light of these facts it seems certain that peptone and Fleischsäure are either identical or closely allied, and that the quantitative formula for the two is represented, at least approximately, in the determined formula for Fleischsäure.

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[1] Archiv f. Anat. u. Physiol., Leipzig, 1894, S. 401; **Zeitsch. f. physiol. Chem., Strassburg,** 1896, Bd. xxi., S. 360.

Frequent reference has been made to the amino-acids formed in tryptic proteolysis and to organic bases (lysin, lysatin, etc.) formed in the hydrolytic decomposition of proteins.

The following are the most important of the cleavage products of the proteins:

Glycin, or aminoacetic acid.
Alanin, or aminopropionic acid.
Phenylalanin, or phenylaminopropionic acid.
Tyrosin, or phenyloxyaminopropionic acid.
Aminovaleric acid.
Leucin, or aminobutylacetic acid.
Aspartic acid, or aminosuccinic acid.
Glutominic acid, or aminoglutaric acid.
$\left.\begin{array}{l}\text{Arginin, guanidinaminovaleric acid}\\ \text{Lysin, diaminocaproic acid}\end{array}\right\}$ the hexon bases.
Histidin.
Cystin.
Ammonia.
Carbon dioxid.
Hydrogen sulphid.

3. **The Lipolytic Enzyme—Lipase.**—Fats are not changed chemically in any of the digestive processes which take place before they reach the small intestine. Adipose tissue, consisting of collagen and fat, is broken up in the stomach by the peptic digestion of the collagen (or gelatin), which releases the fat. Animal fat is fluid at the temperature of the animal body.

The released and fluid fat is mixed with the acid chyme in the form of small globules and passes into the duodenum. The alkaline salts of the pancreatic juice and bile neutralize all free hydrochloric acid and change the reaction to neutral or alkaline in the duodenum.

A simple fat, as tripalmitin, is a combination of three fatty acid molecules with propenyl, the glycerol radical. The general structural formula of the fatty acids of the primary monatomic alcohol series is: $CH_3—(CH_2)_{n-2}—COOH$. The formula of palmitic acid, the sixteenth member of the series, is: $CH_3—(CH_2)_{14}—COOH$; of stearic acid the eighteenth member: $CH_3—(CH_2)_{16}—COOH$. Tripalmitin has the following structural and quantitative formulæ:

$$[CH_3 - (CH_2)_{14} - COO]_3 - C_3H_5, \text{ or } (C_{16}H_{31}O_2)_3 \cdot C_3H_5.$$

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[1] Quoted by Moore from Skand. Arch. f. Physiol., Leipzig, 1896, Bd. v., S. 277.

Oleic acid belongs to the triatomic alcohol series whose acids possess the following general formula: $CH_3—(CH_2)_{n-4}—(CH)_2—COOH$. Oleic acid is the eighteenth member of the series and has the formulæ: $CH_3—(CH_2)_{14}—(CH)_2—COOH$, or $C_{18}H_{34}O_2$. Triolein has the constitution indicated in the formula:

$$[CH_3 — (CH_{2\ 14} — (CH)_2 — COO]_3 \cdot C_2H_5.$$

Animal fat is a mixture of tripalmitin, tristearin, and triolein in various proportions. Certain fats and oils, especially vegetable oils, have various other members of the fatty acid or oleic acid series.

The task which presents itself now is to find the effect of steapsin upon these compounds. Let tripalmitin be taken as a type. Steapsin brings about a hydrolytic cleavage of the molecule into its constituents:

$$[CH_3 — (CH_2)_{14} — COO]_3C_3H_5 + 3H_2O =$$
$$C_3H_5 \cdot (OH)_3 + 3[CH_3 — (CH_2)_{14} — COOH.]$$

Tripalmitin + 3 water = glycerol + 3 palmitic acid.

This hydrolytic cleavage of the fats leads to an accumulation of glycerin and of various fatty acids in the intestine. The presence of the fatty acids induces, or facilitates three important changes in the contents of the small intestine.

(*a*) **Emulsification.**—Oil is emulsified when it is separated into minute globules which are suspended in the medium and remain separate. If the globules remain separate indefinitely showing no tendency to coalesce the emulsion is said to be *permanent;* while in a *temporary* emulsion the oil globules gradually coalesce and rise to the top of the medium. Emulsions may be classified also on the basis of their formation, whether *mechanical* or *chemical*. If an oil be vigorously shaken with a viscous menstruum, such as egg albumen, or a gum or sugar syrup, the division of the oil may be as fine and the persistence of the emulsion as permanent as in the case of a chemical emulsion. The success of this mechanical emulsion will depend largely upon the vigor and the time of the mechanical agitation. A chemical, also called *spontaneous,* emulsion is produced when the conditions are favorable for the formation of soaps in the fat. Under these conditions a fat or oil will very soon be transformed into a permanent emulsion without the help of shaking, without mechanical aid, though the process is hurried if the materials are shaken or stirred. Both fatty acids and alkalies are present; soap is formed and the contents of the small intestine are mixed by the peristaltic action of the intestinal walls. The conditions are thus favorable for both chemical and mechanical action.

(*b*) **Saponification.**—As has already been stated, the conditions favorable to the formation of soap exist in the small intestine. The pancreatic secretion, the bile, and the succus entericus all contain

Na_2CO_3. When a fatty acid and Na_2CO_3 come together, a sodium soap is instantly formed:

$$2CH_3(CH_2)_{14}COOH + Na_2CO_3 = H_2O + CO_2 + 2CH_3(CH_2)_{14}COONa.$$
$$\text{2 Palmitic acid} + \text{sodium carbonate} = H_2O + CO_2 + \text{2 soap.}$$

(*c*) **Reaction.**—The influence of steapsin upon the reaction in the small intestine has only recently come to the attention of physiologists. As stated above, the first effect of the alkaline secretions of the small intestine is to neutralize all the free acid of the chyme, and to make the contents of the small intestine alkaline. The effect of the enzyme is to liberate from the fats a series of fatty acids. These acids, though weak, suffice to give the contents of the small intestine an acid reaction. But, what is of very great importance to the organism, these particular acids do not interfere with the digestive processes going on in the small intestine.

Pancreatic juice or an aqueous extract of fresh pancreas has the power to curdle milk. That the pancreatic juice has the opportunity to curdle milk, even when a full meal is made of that food, is hardly likely.

b. The Action of the Bile.

This secretion contains no enzyme. Its action is, however, very important when taken in connection with the action of the fat-splitting enzyme of the pancreatic juice. The glycerin liberated by the hydrolytic cleavage of the fats is soluble in water and is probably absorbed readily as glycerin; the fatty acids liberated in the process are insoluble in water and have a melting point considerably above the temperature of the blood (palmitin at 62° C., stearin 69° C.). If they are not dissolved they would pass through the alimentary canal unabsorbed. A part of the fatty acids is combined as soap, which is soluble. Of the Na_2CO_3 required for this process the bile furnishes much the greater part. Any fatty acid not combined in soap is dissolved in the glycocholates of sodium and of potassium. When the bile secretion is diverted from the alimentary canal through a fistula a large part of the ingested fat $\frac{1}{3}$ to $\frac{2}{3}$ appears in the feces as fatty acids. Munk[1] found that the absorption of fats of high melting point suffered more than that of fats of low melting point. Now, the fats of high melting point contain a preponderance of stearin, whose acid (stearic acid) has a high melting point (69° C.), and thus resists other intestinal solvents of fatty acids.

Another most important property of the bile salts is their ability to dissolve the soaps of the alkaline earths. Most drinking-water contains calcium and magnesium salts in solution. These salts combine at once with fatty acids to make calcium or magnesium soaps, or they displace Na from the soluble soaps already formed.

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[1] Virchow's Archiv, 1890, Bd. cxxii., S. 302; quoted from Moore.

These soaps of Ca and Mg are insoluble in water, and but for the presence of glycocholate of Na and K would pass out of the alimentary canal unabsorbed.[1]

One of the most important services which the bile renders is *to accentuate the action of the pancreatic enzymes.*

"We shall see that in the favoring action of the bile upon the ferments of pancreatic juice we have discovered the main feature of its digestive importance. Numerous experiments on dogs, systematically carried out, have shown us that when a definite quantity of bile, which varies for the different ferments, is added to pancreatic juice, it produces a constant and decided accentuation of the activity of its enzymes. The effect was most pronounced on the fat-splitting ferment, the action of which was increased twofold or threefold, less on the other two, which were only increased about twofold."[2]

"When we link all these facts together we may with certainty conclude that the chief duty of the bile is to facilitate the transition from gastric to intestinal digestion. It arrests the action of the pepsin, which is injurious to the ferments of the pancreatic juice, and favors the ferments of the latter, in particular the fat-splitting ferment" [p. 158].

One may summarize as follows the action of the bile in the digestive process:

(*a*) *It assists in the emulsification of fats.*

(*b*) *It assists in the saponification of fats.*

(*c*) Its glycocholates and taurocholates assist in the solution of fatty acids.

(*d*) Its salts in solution dissolve the soaps of the alkaline earths (Ca, Sr, Mg, Ba), which are insoluble in water.

(*e*) It acts as a "natural laxative" through lubrication of the feces.

(*f*) It diminishes putrefaction in the large intestine, not by any antiseptic action, but by some other obscure influence.

(*g*) *It reinforces and accentuates the action of the pancreatic enzymes.*

c. The Action of Succus Entericus.

Reference has already been made to the fact that the Na_2CO_3, which makes 0.25 per cent. to 0.5 per cent. of the intestinal juice, assists the pancreatic juice and bile in the emulsification and saponification of fats.

1. **Invertin.**—One of the enzymes of the intestinal juice is the inverting enzyme, *invertin*. This enzyme acts upon disaccharides, and through hydrolytic cleavage resolves them into two co-ordinate monosaccharide molecules. The amylolytic enzymes of the saliva and pancreatic juice change starch to maltose, a disaccharide. The

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[1] Neumiester, Lehrbuch der physiol. Chemie, Jena, 1893.

[2] Pawlow, p. 157.

sugar of milk is lactose, a disaccharide. All of these disaccharides possess the quantitative formula $C_{12}H_{22}O_{11}$.

Experiment has determined that none of these disaccharides appear in the blood. Only monosaccharides appear in the blood. The change from disaccharides to monosaccharides must take place before the sugar is discharged into the portal blood. The intestinal canal possesses in the invertin an enzyme capable of inducing the required changes:

(I) Maltose + H_2O + invertin = invertin + 2 dextrose.
$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6$.
(II) Lactose + water + invertin = invertin + dextrose + galactose.
$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$.
(III) Saccharose + water + invertin = invertin + dextrose + levulose.
$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$.

2. **Enterokinase, a Ferment of Ferments.**—When this enzyme is added to pancreatic juice it doubles the activity of the amylopsin and steapsin and trebles (or more) the activity of the trypsin.

"The succus entericus possesses the striking capability of augmenting the activity of the pancreatic ferments, and more especially the proteolytic. In the case of the latter, the increase often reaches an astonishing degree. He who has once convinced himself of this by experiment will never doubt for a moment that this accentuating influence is the most important function of the succus entericus."[1]

Enterokinase is secreted under the immediate stimulus of food. A remarkable adaptation to dietetic conditions is thus possible.

The proteolytic enzyme is secreted in the form of the zymogen—*trypsinogen*. The active trypsin would digest the other enzymes within the ducts of the pancreas if they were not thus protected. *The first work of the enterokinase is to change trypsinogen to trypsin.* In the lumen of the duodenum the trypsin attacks food proteins and the other enzymes are not injured.

3. FACTORS WHICH INFLUENCE INTESTINAL DIGESTION.

Such factors as cooking, mastication, and temperature have little direct influence upon intestinal digestion. Even the indirect influence is slight, because the pancreatic juice can digest raw starch; the stomach retains the food until the imperfections of mastication are largely corrected; and its sojourn in the stomach certainly gives it the temperature of the body. There are two important factors yet to consider:

a. The Influence of Bacteria upon Intestinal Digestion.

"The food in the alimentary canal is acted upon, not only by the digestive secretions and their enzymes, but to a greater or less number of bacteria increase from duodenum downward

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[1] Pawlow, p. 159.

extent by certain bacteria, which are never entirely absent, although the amount of their action varies greatly under healthy conditions, with the nature of the food, and the class of the animal. Under abnormal conditions the growth of these organisms may be greatly increased, and nutrition be seriously impaired *by the turning to their own uses the products of normal digestion,* and leaving, for the service of the animal, only degradation products inadequate or wholly unsuited for the purposes of its metabolism." (Moore.)

The effect of cooking and of the HCl of the gastric digestion is to practically free the chyme which enters the duodenum of all or nearly all bacterial life. We may look upon the bacteria of the intestinal tract as *parasites* introduced with the food and thriving only moderately when all of the conditions are normal. When the digestion is deranged the conditions may be favorable to the excessive development of various bacteria (organized ferments) whose food is robbed from the host and whose excreta may be extremely deleterious to the host. It has been contended that these parasites are "*beneficial;*" a similar contention might be made in behalf of certain vermin (!) *Parasitism is not beneficial to the host.*

Nuttall and Thierfelder[1] have demonstrated that young animals with sterile alimentary tract, sterile air, and sterile food grow just as well as the control animals under the usual conditions. This applies as well for vegetable foods as for animal foods. Animals live and thrive in spite of their bacterial parasites, and not because of them.

The action of bacteria may be discussed in its relation to different parts of the alimentary tract, and in its relation to different foodstuffs.

1. **The Action of Bacteria in Different Parts of the Alimentary Canal.**—(*a*) **Bacteria of the Mouth** have no influence upon intestinal digestion, though they may menace the teeth of the animal.

(*b*) **Bacteria of the Stomach** are introduced with the food and, as mentioned above, are usually destroyed by the HCl when that acid is sufficiently strong (0.2 per cent. to 0.3 per cent.). When the HCl is very weak, much delayed in secretion, or wholly absent, the development of *bacterium lactis* and various fermentive and putrefactive forms is favored. In the case of *B. lactis* one might make an exception to the statement made above that bacteria and their excreta are not beneficial. Peptic digestion can only proceed in the presence of an acid. Lactic acid can take the place of HCl in forming acid albumin or syntonin. In the absence of HCl lactic acid, the excreta of *B. lactis* may be advantageous to the system.

(*c*) **Bacteria of the Small Intestine.**—The acid reaction of the chyme representing free HCl and acid albumin is neutralized and replaced with an acid reaction due to the accumulation of organic acids. At first these organic acids are fatty acids released by steapsin from neutral fats; these are, however, absorbed as absorption progresses; the acid reaction arising from this source will tend to decrease. But it has been observed[1] that the acid reaction usually found at the lower end of the ileum in man is due principally to *acetic acid,* with only traces of fatty and other acids. It seems likely that, in the small intestine, the acidity due to fatty acids is replaced from above downward by acidity due to fermentation of carbohydrates. Moore and Rockwood,[2] in a very extended and recent series of observations upon the dog, cat, white rat, guinea-pig and rabbit, conclude: (I) "The reaction is not normally acid throughout the entire length of the small intestine, and the alkalinity increases in passing down the intestine." (II) "The presence of fat in the food causes in carnivora an acid reaction which persists until the lower third of the intestine is reached." (III) "The alkalinity is much greater in herbivora than in carnivora; . . . also, in carnivora the alkalinity is markedly increased by carbohydrate food." (IV) "It is probable that in the animals observed any extensive bacterial decomposition of carbohydrates that may occur takes place in the large intestine."

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[1] Zeitsch. f. physiol. Chemie, 1895, Bd. xxi., S. 109.

(*d*) **Bacteria of the Large Intestine.**—In this segment of the alimentary canal the reaction is conceded by all to be *alkaline,* due to the neutralization of any acid entering the cæcum by the distinctly alkaline secretions of the mucous membrane. In the large intestine profound changes take place under the influence of putrefactive bacteria. The proteins are especially attacked in this segment of the canal, the acid reaction of the small intestine protecting them normally from putrefactive changes in that portion of the canal.

2. **The Action of Bacteria in Relation to Different Foodstuffs.**—(*a*) **Bacterial Action on Carbohydrates** consists (I) in the fermentation of the *sugars* with the formation of ethyl alcohol, acetic, lactic, butyric, and succinic acids, with the liberation of CO_2 and H; (II) in the decomposition of *cellulose* with the formation of marsh gas $(CH)_4$ and CO_2; (III) in the decomposition of *starch* with products similar to (I). The fermentation and decomposition of carbohydrates begins in the small intestine and progresses with increasing activity through the cæcum, then with decreasing activity to the rectum.

(*b*) **Bacterial Action on Proteins** seems to be inhibited by the acid reaction of the small intestine. As soon as the contents of the alimentary tract become alkaline the decomposition of proteins is facilitated. There are two series of products formed during the putrefaction of proteins and the proteolytes. The members of the first series are derived from tyrosin in the following manner:[3]

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[1] Macfadyen, Nencki, Sieber, Arch. f. exp. Path. u. Pharmacol.

[2] Jour. Physiol., 1897, vol. xxi. p. 373.

[3] Baumann, Berichte d. deutsche chem. Gesell., 1879, Bd. xii., S. 1450.

[illegible]

gases formed are carbonic acid gas - H, H_2S
and methyl mercaptan

$$C_6H_4{\cdot}OH - CH_2 - CHNH_2 - COOH + H_2 = NH_3 + C_6H_4{\cdot}OH - (CH_2)_2 - COOH.$$

$$\text{Tyrosin} + H_2 = NH_3 + p\text{-oxyphenylpropionic acid.}$$

P-oxyphenylpropionic acid parts with CO_2 and becomes *p*-ethylphenol ($C_6H_4 . OH - C_2H_5$), which has not, however, been found in the intestine, though it occurs in experiments *in vitro*; *p*-ethylphenol next becomes oxidized (+3O) to *p*-oxyphenylacetic acid. This in turn gives up CO_2 and becomes *p*-cresol (*p*-methylphenol), which is again oxidized to *p*-oxybenzoic acid—not yet found in the intestine.

Oxybenzoic acid gives up CO_2 and forms phenol (C_6H_5OH), which is usually joined to sulphuric acid for excretion.

The second series of products includes *Indol* and *Skatol*, or Methylindol. Both of these bodies are soluble in water, from which solution they crystallize in small scales. Both are in part absorbed and in part passed out with the feces. They will be discussed under Metabolism and Excretion. Not derived from Tyrosin

b. The Influence of Cellulose upon Intestinal Digestion.

In the case of herbivora it has been demonstrated by Bunge[1] that cellulose is important, not as a nutrient, but "in giving bulk and looseness to the food and in mechanically inducing peristalsis by irritation of the mucous membrane." To the herbivora it is indispensable; to omnivora, like man, it is advantageous in moderate quantities; to carnivora it has no advantages. Herbivora digest 60 to 70 per cent. of it, man 4 to 60 per cent. according to the condition of the cellulose. Under the influence of bacteria it is subjected to a hydrolytic cleavage represented in the following equation:

$$[C_6H_{10}O_5 + H_2O = 3CO_2 + 3CH_4]_n.$$

The reaction is varied by the production also of acetic, propionic, butyric, and valerianic acids.

4. THE REMNANTS OF INTESTINAL DIGESTION.

The Feces.

The feces represent that part of the contents of the alimentary tract which is not absorbed into the circulation. The contents represent not only the ingested food, but portions of various secretions and of excretions, besides bacteria and their excreta, and epithelial elements from the mucous membrane. The bulk of the feces is modified by the proportion of indigestible material in the ingesta. The feces of the herbivora are very copious, while those of carnivora are comparatively scanty. In man the weight will vary from 170 gms. to 400 to 500 gms., according to diet. The amount of water varies with the character of the food and with the habit of the animal, free and frequent passages having more water than those associated with constipation. The longer the fecal matter is retained the larger the proportion of water absorbed from it.

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[1] Physiologische Chemie, 1894, S. 75.

The composition of the feces may be classified thus:

Composition of the Feces

- GASES. N, H, CO_2, H_2S, CH_4.
- LIQUIDS. H_2O (68 % to 82 % normally).
- SOLIDS:
  - *Undigested food.* Fats, fragments of meat, starch.
  - *Indigestible matter.* Cellulose, ligaments from meat, keratin, mucin, gums. and the resins.
  - *Bacteria* and *Products* of their decomposition of foods: Lower fatty acids, lactic acid, tyrosin and its decomposition products, phenol.
  - *Soaps* of Ca and Mg.
  - *Bile residues.* Mucus, cholesterin, biliary acids, stercobilin.
  - *Excretin.* $C_{78}H_{156}SO_2$.
  - *Inorganic salts.* Soluble salts of Na, K., Mg, etc.
    Insoluble salts of Ca, Mg, Fe, etc.

5. THE MOVEMENTS OF THE INTESTINES.

The movements of the intestines are together called *peristalsis.* Peristalsis consists of a progressive wave of contraction which usually passes from above downward. This wave of contraction involves especially the circular fibres, whose progressive contraction has the mechanical effect of sliding a small ring along the gut contracting the lumen upon the contents. Accompanying the contraction of the circular fibres and just preceding it is a contraction of the longitudinal fibres. This combined *vermicular peristalsis* is very effective in pushing on the contents of the canal.

The peristalsis of the intestinal tract is stimulated by the presence of food in general; but it is especially stimulated by the presence of such sharp pieces of cellulose as occur in coarse meals of the cereals. The vagus seems to be the efferent nerve. Section of the vagus causes cessation of all reflex peristalsis. Section of the splanchnics causes vasodilatation with profuse secretion of the succus entericus.

The opening of the pylorus is governed by the duodenal mucous membrane, apart altogether from the fulness of either stomach or duodenum. The efficient stimulus is the reaction of the upper duodenum: if this is acid in reaction the pylorus closes; if it is alkaline, the pylorus opens.

So when the acid contents of stomach are allowed to pass into the duodenum the pylorus closes and holds back the acid flood, while the presence of acid in the duodenum stimulates and increases the secretion of pancreatic juice, which in turn neutralizes the contents of the duodenum; then the pylorus opens and allows a fresh lot of acid chyme to pass through.

6. DEFECATION.

Ingestion begins with a voluntary act and is consummated with an involuntary act. Egestion or defecation begins with an involuntary and is consummated with a voluntary act.

As the food approaches the rectum it gradually loses water and greater force is required to move it along the canal: accordingly the circular muscular coat is thicker in the lower end of the canal, reaching a maximum in the external sphincter of the anus.

The slow contractions of these muscles gradually advance the feces to the rectum, where their accumulation periodically stimulates a strong expulsatory contraction of the circular muscle fibres of that viscus. This, though purely involuntary, is not outside the consciousness of the individual. The final conscious act consists in voluntarily inhibiting or suspending the tonic contraction of the external sphincter. In the absolutely typical and normal condition the contraction of the walls of the rectum suffices to rid it of the accumulated feces. Frequently the force of these muscles must be supplemented. This is accomplished by a voluntary contraction of the abdominal muscles, which causes a high pressure within the abdominal cavity, the intravenous pressure in the hemorrhoidal veins is positive, and there is a tendency for these veins to become permanently distended, causing hemorrhoids.

PATHOLOGIC PHYSIOLOGY OF DIGESTION.

A. SALIVARY DIGESTION.

1. THE SECRETION.

a. Increased Secretion.

Through various influences the secretion of the salivary glands may be increased, not only during the process of mastication, but during periods when no food is taken. It is especially in the latter instance that the harmonious co-ordination of glandular activity in the digestive act is disturbed and ill effects result.

1. **The Causes.**—The causes of such overactivity may be classed as those acting (*a*) LOCALLY—*i. e.*, directly upon the gland tissue or nervous mechanism: Of these the most important are: (1) Certain sialagogues like pilocarpine, physostigmine, mercury, and potassium iodide. In mercurialism the stomatitis produced by the mercurial compounds secreted in the saliva no doubt also augments the gland-

ular activity in a reflex manner. (II) Certain products of metabolism isolated by Bouchard[1] from the alcoholic extract of the dry urinary residue are doubtless the cause of the salivation in uræmia, as observed by A. Robin[2] and others.

(β) REFLEXLY.—(I) Not alone may the origin of such impulses find their cause located in the oral cavity, as a stomatitis, glossitis, gingivitis, or more direct irritants like a trauma, dental eruption, regurgitated gastric contents, acids, ether vapors, and tobacco smoke, but (II) may be seated in more distant viscera, like a pregnant uterus, an inflamed pancreas, or an ulcerated stomach, and even in the peripheral nerves of the cutaneous expanse, as in some cases of trifacial neuralgia. -

(γ) CENTRAL.—Morbid cerebral impulses are often the only cause for the salivation sometimes observed in cases of hysteria and neurasthenia and irritative nuclear phenomena are probably the explanation for the ptyalism in bulbar paralysis and rabies.

2. **Effects.**—THE EFFECTS OF HYPERSECTION manifest themselves (α) LOCALLY—*i. e.*, in the oral cavity, where accumulations of watery saliva give rise to a constant feeling of discomfort, which becomes most troublesome when attempting to speak, necessitating frequent acts of swallowing or expectoration. If the mouth muscles are paralyzed, as in bulbar paralysis and facial palsy, or the reflex mechanism of deglutition is interfered with, as in comatose states, the saliva flows continuously from the mouth, and constitutes what is known as ptyalism.

(β) ON DIGESTION.—(I) *Salivary digestion* may be disturbed in the stomach on account of the great dilution from the admixture of mucus, and sometimes the total amount of ptyalin poured out upon the amylaceous food may actually be diminished. (II) *Gastric digestion* is effected in various ways. The diminution of the appetite usually present leads to a diminished secretion of gastric juice. The large volume of aqueous saliva dilutes the small quantity of gastric juice finally secreted. The alkali contained in the saliva continually poured into the stomach neutralizes the HCl. The mucus introduced impedes mechanically the processes of peptic digestion. Substances sometimes excreted in the saliva act as irritants for the gastric mucosa. The bacteria often present in the mouth infect the gastric contents.

(γ) SYSTEMIC EFFECTS most often observed in prolonged salivation result from the disturbances of digestion; the constant feeling of discomfort often resulting in loss of rest and sleep; the loss of water by the mouth, which in extreme cases may amount to several litres, but above all to the underlying pathologic causes.

b. Diminished Secretion.

1. **Causes.**—In various ways the secretion of saliva may be diminished—viz.: (*α*) ALTERATIONS IN THE GLAND SUBSTANCE are rarely the cause of a complete suppression of secretion, unless this phenomena in febrile disturbances is sometimes due to such alterations. The function of gland parenchyma destroyed by inflammatory or neoplastic processes is soon vicariously assumed by the remaining glands.

(*β*) LOSS OF BODY FLUIDS, and associated blood concentration, such as is observed in severe diarrhœa and dysentery, cholera, diabetes, and chronic nephritis, lead not only to a diminution of the salivary secretion, but to a concentration of all other glandular products.

A similar phenomenon is observed in fevers, and can partially be attributed to the loss of water by other channels, as the lungs, owing to more frequent respirations and greater heat of the expired air, and through the skin by augmented perspiration.

(*γ*) DISTURBANCES IN THE NERVOUS MECHANISM at various parts doubtless frequently play a role in reduced activity of the salivary glands. (I) The paralytic effect of the atropine series of alkaloids on the peripheral endings of the chorda tympani is a well-established pharmacologic fact; (II) that lesions of the chorda result in a similar effect is substantiated by clinical evidences, and (III) it seems reasonable to presume that the sympathetic supply is subjected to the same vasomotor impulses which underlie the general fall of blood pressure in such diseases as shock, Addison's disease, or even prolonged febrile disorders. (IV) Central involvement is suggested by Hadden[3] to be the cause of xerostomia (dry mouth) in that condition first described by Jonathan Hutchinson.

(*δ*) DUCT OBSTRUCTION, resulting either from compression, stricture, or calculus, may rarely be the cause of suppression from a single gland, and often irritations thus produced reflexly bring about overactivity in the remaining glands.

2. **Effects.**—The effects of diminished salivary secretion are noted: (*α*) LOCALLY, where they result in desiccation of the oral mucous membrane.

The thirst usually experienced by fever patients can in part be attributed to this result; hence, it is often greatly moderated by keeping the mouth moist, as by sucking a piece of ice. The appearance of the tongue, often glazed, coated, and fissured, which in some febrile disorders constitutes an important part in the clinical picture, is also chiefly dependent on the deficiency of moisture.

(*β*) DIGESTIVE DISTURBANCES.—Deficient in salivation results in difficult mastication, with a failure to convert the particles of food into a soft pulp, and trouble in swallowing because without sufficient flow of water clearing of the throat becomes impossible, and the passage of the bolus through the pharynx and œsophagus is difficult and painful.

The action of the amylolytic enzyme is impeded by deficient admixture with water; hence salivary digestion rarely begins in the mouth, and, because of the diminished quantity of ferment secreted, cannot be very active in the stomach.

Gastric digestion is effected by the loss of appetite and perversion of taste which accompanies excessive dryness of the mouth; also by the insufficient mastication and bolting of the food.

(γ) SYSTEMIC EFFECTS are not due to derangements of salivary digestion, but are dependent chiefly on the pathologic cause underlying the perversion in secretion, as is noted in typhoid fever; where desiccation of the mouth occurs as soon as unconsciousness results.

The constant thirst, anorexia, and resultant gastric disturbances doubtless are an important factor in producing malnutrition in these cases.

c. Abnormal Composition.

Due to the constant admixture with buccal secretion, it becomes possible only to study the mixed saliva.

1. **Reaction.**—The reaction is frequently altered. Sometimes by products of bacterial multiplication in the mouth. Such a hyperacidity leads not only to irritation of the oral mucosa and its consequences, but when more concentrated and circumscribed in its action becomes the underlying cause of dental caries. More often the acid reaction is due to acid phosphates secreted by the glands. This is observed in many cases of diabetes mellitus, and occasionally in other constitutional disorders. The following observations were recently reported by Stern and Lederer:[4] Of 20 cases of acute gastritis, 40 per cent. showed acid reaction; 182 cases of hyperchlorhydria, 39 per cent.; and of 23 cases of hypochlorhydria, 9 per cent. showed similar reactions. Often in these cases the reaction was found to be amphoteric, and frequently the acid reaction was due to lactic acid. That the alkalinity is constantly increased in some individuals is demonstrated by the persistent tendency to deposit earthy phosphates in the form of tartar on the teeth and that the same reaction is at times constantly present in the unmixed salivary secretion becomes evident from a case of salivary duct calculus recently carefully studied by Roberg.

The relationship of phosphatic deposits on the teeth in pernicious anæmia and altered reaction of the salivary secretions remains to be demonstrated.

From recent studies by Michaels,[5] Kirk,[6] and Kyle,[7] it seems that alterations in reaction of the oral and nasal secretions are a factor in the production of the symptoms of hay fever, an excess of fixed alkali leading to the liberation of NH_3, on the surface of the mucous membrane, from an excess of ammonia salts contained in the secretions of these individuals; while free acids result in the separation of the SCN radical from its K combination. These radicals liberated give rise to irritative phenomena *in loco.*

2. **Ptyalin.**—The amylolytic enzyme may be greatly diminished in a measured quantity of salivary secretion, while the total amount secreted in twenty-four hours may even be actually increased. The saliva in many cases of ptyalism having the same character as that produced by stimulation of the chorda tympani, becomes poorer in solid constituents the longer stimulation lasts. An actual diminution of this ferment is associated most frequently with reductions in the total salivary secretion and is most common in febrile disturbances.

3. **Mucus.**—A product of both salivary and buccal glandular activity is thus increased most markedly in catarrhal affections of the oral mucosa and by the action of local irritants, like ether vapors and tobacco smoke, whereby local and reflex influences the mucous glands are stimulated, and the surface epithelium undergoes mucoid degeneration and desquamation. It is in this way that epithelial cells become a constant admixture of such secretions.

Often large volumes of mucus enter the mouth from adjoining cavities, such as the pharynx, trachea, and nares.

Although the sublingual gland is a mucous gland it is extremely rare for increased amounts of mucus to be the product of this organ, because the abnormal stimuli give rise to a secretion poorer in solid constituents; and even if rarely the amount of mucus should be increased it would be greatly diluted by the watery secretions poured out by the other salivary glands acting simultaneously.

4. **Abnormal Constituents.**—(*α*) SUBSTANCES OF EXOGENOUS ORIGIN, like ingested mercury and lead compounds or potassium iodide, are excreted into the mouth, where they once more show their irritant properties, the mercury giving rise to a severe form of stomatitis associated with characteristic *fœtor ex ore* and loosening of the teeth, while the lead salts show themselves most at the edges of the gums, where they come in contact with sulphides liberated in decomposing protein foods and are deposited in the form of black-lead sulphide. This deposit arranged in a linear manner gives rise to the well-known Burton's line in these chronic intoxications.

The potassium iodide re-excreted in the saliva gives rise to a persistent unpleasant taste, leading finally to perversion of appetite which helps to aggravate the digestive disturbances already inaugurated.

(*β*) METABOLIC PRODUCTS like urea have been found in the saliva in cases of renal insufficiency; uric acid was found in 21 of 59 cases of uricacidæmia examined by Stern and Lederer,[9] while glucose was found in 46 per cent. of 181 cases of diabetes mellitus examined by the same observers. The normal saliva and buccal mucus are not bile stained in cases of icterus, while in diseased conditions of the glands like mercurial ptyalism the secretions assume an icteric hue. (Rolleston.[8])

(γ) Potassium Sulphocyanide.—The absence of this salt was recently put forth by German clinicians as a constant symptom of carcinoma ventriculi, but other clinicians have also found it absent in various other gastric disorders. Too little evidence is at hand to give a final conclusion on the diagnostic significance of this symptom, or the "Rhodan Kalium Reaction." From recent studies of hay fever it appears that sulphocyanides are increased in these patients and liberated on the mucous membrane by acid action.

(δ) Toxins.—These are doubtless often present in the mixed saliva, and the virus of rabies seems to be most infectious when contained in this fluid. The admixture of secretion from mucous patches makes the mouth fluid extremely virulent in syphilis.

d. The Buccal Fluid.

1. **Increased.**—Because the innervation of these glands is not well understood, we cannot classify the causes giving rise to perversions of activity as to their mode of action. Many irritants which result in hypersecretion on the part of the salivary glands have a similar effect upon the mucous glands, and the salivation produced is a result of the combined glandular activity.

Local irritants are, however, most effective in stimulating the mucous glands, as is seen in the various forms of stomatitis. Here the products of bacterial activity, as the abundant acids produced by oidium albicans, the acids resulting from saprophytic multiplication in retained food morsels, and toxins formed by pathogenic organisms, play an important part. Many chemicals stimulate these glands. The more specific inflammatory processes like ulcerative or gangrenous stomatitis, glossitis, and the gingivitis seen in scurvy or following the mechanical action of deposited tartar on the teeth all reflexly lead to a hypersecretion of mucus.

2. **Diminished.**—A suppression of buccal secretion is present in most cases where the saliva is diminished, but is most evident in prolonged fevers, like typhoid, where extreme dryness of the entire mouth prevails.

That the innervation of the glands corresponds with that of the salivary glands, at least in part, is demonstrated by the dry mouth in atropine poisoning.

Duct obstruction leads sometimes to cystic dilatation of one or more of these glands, and if such a dilated gland is located near the frænum linguæ it gives rise to one of the clinical forms of ranula.

2. MOTOR DISTURBANCES.

a. Mastication.

1. **The Causes.** (*α*) Mechanical Defects.—These may, various ways, seriously impede mastication.

(i) Absence, defects, or irregularities of the teeth are the commone occurrences in civilized man. (ii) Defects in the palate and chee the result of ulcerative or carcinomatous destruction and congenit anomalies, as cleft palate and harelip are often met with. (ii Fractures and dislocations of the maxilla and ankylosis of the inferio maxillary articulation may render mastication impossible.

(*β*) Alterations in the Musculature, leading to disturbance of mastication, are oftenest found in the tongue in the form of diffuse inflammatory changes (glossitis) or carcinomatous infiltration. In noma sometimes great portions of the cheek muscles are destroyed.

(*γ*) Disturbances in Innervation are frequently the cause of difficult mastication. Through central impulses chewing may be rendered impossible in painful affections of the mouth, like an alveolar or peritonsillar abscess, angina, or parotitis. But the nerve supply to the part is more often at fault. The paralysis of certain muscles seriously interfering with mastication, as the buccinator and orbicularis oris in facial paralysis, the tongue muscles in hypoglossal paralysis, and the strong masticatory muscles by lesions in the inferior maxillary division of the V nerve.

Sensory paralysis makes mastication difficult, as is seen when the surface of the buccinator becomes anæsthetic and in certain cases of hæmianæsthesia.

(*δ*) The Secretions of the Mouth, as has been previously indicated, play an important part in the subdivision of food particles.

2. **Effects.**—(*α*) Mastication may Become Impossible when extensive congenital defects prevail, or when the tongue has undergone serious anatomic changes and in the presence of extremely painful local affections, bilateral muscular paralysis, ankylosis, dislocations or fractures of the maxilla.

(*β*) Difficult Mastication is observed when the oral mucosa is partially anæsthetic or few important muscles like the buccinator and orbicularis oris are paralyzed; also when the innervation of many of the masticatory muscles is affected, as in cases of bulbar paralysis.

In buccinator paralysis from failure to compress and contract the cheeks, food accumulates between the cheek and gums and is not kept well between the teeth during mastication.

In orbicularis paralysis the mouth cannot be closed and may allow portions of food to escape.

In the slowly progressive bulbar paralysis (Wachsmuth) with symmetric nuclear lesions, where the tongue is usually early affected, it loses its function of retaining food between the teeth, and lies as a motionless and atrophic mass on the floor of the mouth. With unilateral lesions motor disturbances are not so marked and to the observer become evident when upon protruding the organ it deviates distinctly to the paralyzed side.

(γ) IMPERFECT MASTICATION is most frequently the result of dental defects, but may be caused by incomplete insalivation or hasty habits at eating. Often when chewing is difficult imperfect subdivision in the mouth is the result.

Food thus imperfectly insalivated and bolted offers serious impediment to active digestion in the stomach.

b. Deglutition.

Derangements of this complex act may best be considered by analyzing its various phases.

(*a*) VOLUNTARY PART.—All of the paralytic phenomena affecting mastication must necessarily influence the *formation of the bolus*, and lesions of the hypoglossal are most effective to produce difficulty in moving the food mass on to the pharynx.

(β) INVOLUNTARY PART. *Pharyngeal Deglutition.—The causes* of interference with the transit of food through the pharynx may at times be a *simple mechanical one;* as defects congenital or acquired in the soft palate or epiglottis and actual obstruction by neoplasms, enlarged tonsils, and retropharyngeal accumulations of pus; or by a foreign body, as an intubation tube in the larynx, interfering with the muscular coaptation; but more frequently results from *derangements in the complex nervous mechanism.*

Centric disturbances exclusive of nuclear lesions are the underlying condition in this symptom when seen in deep coma and hysteric states. The spasm seen in rabies results from the concentrated condition of the virus in the medulla. But nerve changes are a much commoner cause, the efferent tracts being bilaterally involved in bulbar paralysis, while in the neuritis accompanying diphtheria the transmission of sensory impulses is also interfered with.

Through painful afferent impulses from an angina, peritonsillar or retropharyngeal abscess, the act is sometimes partially inhibited. Muscular changes, although present in severe diphtheria and other inflammatory affections of the throat, are rarely the sole or primary cause. Baginsky claims that early diphtheritic paralysis is due to myositis.

The effect is a disturbance in one or more of the three parts of the act.

The transportation of food into the œsophagus is impeded chiefly by painful local conditions, is interfered with when other exits like the posterior nares or the oral cavity remain open, but it is not at all affected by the pharyngeal anæsthesia which prevails in many cases of hysteria.

The guarding of the posterior nares is interfered with in all affections of the soft palate, and food is regurgitated through the nose. Solid particles may become lodged in the nasal cavity and set up painful inflammation.

Guarding the laryngeal opening is a very important phase in deglutition, and when it is interfered with food morsels, fluids, or even the infected mouth secretions have free access to the respiratory passages and may give rise to obstruction or lead to irritative phenomena not only in the bronchial tube, but often in the depths of the lung parenchyma. Hence, such accidents are always to be feared in comatose states like ether anæsthesia and severe infectious disease, while in hopeless paralytic and marantic states, by producing an inhalation pneumonia they may quietly close the scene.

(γ) Œsophageal Deglutition speedily executed in health may in various ways be interfered with, thus inhibiting or preventing the entrance of food into the gastrointestinal tract.

(1) *The cause* is most frequently a purely *mechanical disturbance*, as *defects* in the continuity of the tube. These may result from perforation, proceeding from without, as suppurative processes surrounding it, or from within, as by the lodgement of a foreign body or passage of a stomach tube, but mostly by ulcerations starting in the wall, as carcinoma, peptic and typhoid ulcers; or by the action of caustics.

Diverticula may arise in two ways: *By traction* caused by adhesion of diseased neighboring structures, and are located near the bifurcation of the trachea. *By pressure from within.* These arise most commonly from the posterior wall of the upper portion, and result from congenital defects or thinning of the muscular coat and hernious protrusion of the mucous membrane.

Strictures are the most common cause of dysphagia and may result from a purely *intrinsic* condition like a neoplasm, but more often from *changes in the wall*, as a muscular spasm or a cicatrix, resulting from inflammation, corrosion, or trauma; also frequently due to cancerous invasion. *Compression from without;* by neighboring neoplasm, aneurysm, goitre, lymphatic glands, or even a distended œsophageal diverticulum; while the *lodgement of a foreign body*, either in the narrowest parts of the normal gullet, as opposite the cricoid cartilage and tracheal bifurcation, or at the cardia and diaphragmatic ring, or at a point of pathologic stenosis, is not an infrequent condition.

The nervous mechanism is at fault in those cases of idiopathic dilatation where the condition resembles the effect of bilateral *section of the vagus*, experimentally demonstrable in animals. Here the gradual and fusiform distention of the gullet, entirely independent of stricture or muscular alteration, becomes a prominent symptom in both instances. *Central impulses* lead to œsophageal spasms in rabies; and most spastic stenoses and the "globus" sensations are manifestations of hysteria. On account of the comparative insensibility of the gullet mucosa, otherwise painful affections seated here inhibit but slightly the swallowing act.

(II) *The effects* vary with the severity and duration of the cause and manifest themselves in *local variations;* from perversions in the course of the food bolus. By unnatural orifices it may find its way into *attached diverticula,* there to decompose, give rise to pressure effects, and periodically to be ejected; or by perforation and rupture *becomes lodged* in adjacent tissues and even enters and fills the adjoining body cavities, setting up violent necrotic inflammation. Such a catastrophe is ushered in by retching, nausea, and vomiting, soon followed by agonizing substernal pain, ending within twenty-four hours, often in severe shock, by interference with the respiratory mechanism.

Or its passage may be partially or completely obstructed. Food swallowed may with difficulty and effort be forced on into the stomach, and frequently *accumulates* in the secondarily dilated œsophagus, and is later slowly forced through the narrowed canal into the stomach, but is more often regurgitated into the mouth.

The severity of the dysphagia thus resulting is largely dependent on the degree of stenosis. When this is moderate, large pieces only are impeded; but when it becomes extreme, even the passage of liquids may be arrested.

The mixture of food thus retained at the body temperature at first undergoes salivary digestion, but later from saprophytic multiplication becomes acid and decomposed. Catarrhal œsophagitis results, which augments not only the substernal pain and oppression, but also causes the hypertrophic musculature to become atonic. Rarely the onward course of the bolus is impossible on account of spasm involving the entire tube, while in idiopathic dilatation distressing food accumulations finally result in organic muscular atonicity.

The constitutional disturbances are chiefly dependent upon the *malnutrition* which results from the insufficient nourishment that arrives in the stomach in the more prolonged cases of severe stenosis. But in some cases of cancer and mediastinal disease the *cachexia* is advanced before dysphagia results, while the gangrenous inflammation set up by ingesta escaping through abnormal orifices causes a profound toxæmia, which, in conjunction with the shock from the accident, tends to a rapidly fatal termination.

B. GASTRIC DIGESTION.

1. THE SECRETIONS.

The gastric secretion is far more important than the saliva, on account of its prolonged action on the ingested food, and hence variations in its quantity and changes in its composition become of the utmost clinical importance.

a. The Hydrochloric Acid.

On account of the complex processes concerned in its production hydrochloric acid is the most subject to variation.

1. **Increased: Hyperchlorhydria.** (*a*) **Cause.**—The cause of such an overproduction is most commonly dependent (*α*) UPON NERVOUS DERANGEMENTS, most of which are but poorly defined.

As examples may be mentioned the high percentage of HCl, which is a characteristic feature in the symptom-complex of hyperchlorhydria, the most common gastric disorder. In the experience of Einhorn,[10] the gastric disorders accompanied by alimentary hyperchlorhydria formed more than one-half of the cases applying for treatment. In this disease the hyperchlorhydria only follows the taking of food, and becomes most marked at the height of digestion.

A continuous secretion of a highly acid gastric juice is seen in the condition first described by Reichmann[11] and later carefully studied by Riegel.[12] The abundant flow may occur periodically (*gastrosuccorrhœa continua periodica*) or continue over longer periods of time (*gastrosuccorrhœa continua chronica*).

An anatomic substratum has not been established for any of these forms of secretory derangements, and since they are most commonly seen in young, active, nervous persons, and in individuals under great mental strain, they are considered as pure neuroses, probably dependent upon abnormally irritated nerve tracts concerned in the secretion of HCl.

Von Noorden[13] is inclined to believe that a hyperæsthesia of the secretory centre may be responsible for the hyperchlorhydria in chlorosis. In 72 of 122 cases of this disease reported by Von Noorden,[13] von Leube,[14] and Hayem,[15] the HCl was increased.

That hypersecretion may result from reflex impulses was demonstrated by Riegel[16] in cases of cholelithiasis and by others in renal colic. Of the hyperchlorhydria often present in the gastric crises of tabes, morbid spinal impulses are doubtless the cause.

(*β*) ASSOCIATED WITH ANATOMIC CHANGES is the hyperchlorhydria of round ulcer of the stomach, which may even continue through the early stages of carcinomatous transformation. The theory that in these indolent ulcers the hyperchlorhydria is more often the cause than the effect is substantiated by clinical observations of von Leube and experimental results of Fütterer.

Von Leube[17] also calls attention to the fact that some of the clinical cases of Reichmann's disease associated with a mild degree of motor insufficiency may be cases of moderately constricted pylorus from scars of healed ulcers, the excessive secretion of HCl continuing.

(*b*) **Effects.**—The effects of excessive amounts of HCl are most pronounced in neurotic individuals, but even in the robust they may lead to serious disturbances.

(1) IN THE STOMACH the hyperchlorhydria has a twofold effect upon (*α*) DIGESTION. (I) *Salivary digestion* is inhibited much earlier and more effectively in those cases where the abundant HCl is poured out only after the ingestion of food; while in the cases of continued secretion the reaction of the gastric contents at no time is favorable for the action of the ptyalin.

(II) *Proteolysis* is actually augmented, as is seen when the gastric contents, after the ingestion of a mixed meal are inspected at the height of digestion. Here it is found that the carbohydrate elements of the meal, like the bread, are but slightly altered, while the protein portion, like the meat, is practically disintegrated.

(*β*) THE MOTILITY OF THE STOMACH may remain good for long periods and (I) may even be *increased*. In such cases it is often found that the stomach is completely empty in one hour after taking a light meal, like an Ewald test breakfast, which consists of two slices of dry bread, 60 gms., and a glass of water, 300 c.c.

(II) In long-continued pronounced cases the almost constantly present superacidity ultimately may set up inflammatory changes in the gastric mucosa, which finally extend to the muscularis, and result in *motor insufficiency*. But this symptom is more frequently dependent upon the constant overloading of the stomach to satisfy the unnatural appetite, which is so often present in hyperchlorhydria.

(III) *Vomiting* may occur in the severer cases at the height of the pain, and is sometimes brought on artificially by the patient to relieve him of great distress. In chronic hypersecretion the excessive acid contents of the stomach may be vomited at night or early in the morning.

When motor insufficiency supervenes, the copious vomiting of sour food masses only brings relief from the excruciating pains which accompany the spasmodic action of the gastric musculature to overcome the pylorospasm, which is usually the determining cause.

(IV) *Pylorospasm* of intermittent duration is not an infrequent accompaniment of superacidity, and brings forth an hypertrophy of the muscular coats of the stomach with which to overwhelm spasmodically its obturation effect. When nerve endings are exposed, as in round ulcer, the summation of stimuli may be sufficient to bring about a more or less continuous spasm of the pylorus, later even resulting in hypertrophy of this muscular ring.

(v) *By relaxing the cardia* and regurgitating or belching small quantities of fluid at frequent intervals, is a way in which the stomach often attempts to rid itself of its irritating contents. As a result thereof the action of the acids is spread to the œsophagus, where it gives rise to substernal burning (pyrosis, or heartburn), and to the mouth and pharynx, where it is recognized by the sour taste and odor.

Large volumes of gas escaping simultaneously may have been swallowed, but oftener are the products of fermentation.

(γ) SENSORY DISTURBANCES in the form of a feeling of pain or discomfort at the height of digestion are the most constant, and often the only effect of the *excess of acid* upon the stomach. They are much influenced by the quantity and composition of the food, appearing early and becoming intense with a coarse vegetable diet, and occurring later with a meal rich in albumen.

The pain when present may be allayed by the ingestion of alkalies, albuminous food, or copious draughts of water, the alkali combining with the HCl to form a neutral salt, the albumen also neutralizing the free HCl forming syntonin or combined HCl, the water diluting the strongly acid gastric contents, thus postponing the irritant effects, even up to the time of the next meal.

The painful sensations may become more intense and of a burning and gnawing character, and be established soon after the ingestion of food when an ulcer is present, and more periodic and cramp like when due to spasm of the pylorus, or irregular and active contractions of the gastric muscularis.

(2) UPON THE INTESTINES hyperchlorhydria has such marked and constant influences that Illoway has recently put forth the hypothesis that the intestinal derangement is the underlying cause of the hypersecretion rather than the effect. (*a*) THE SECRETIONS poured into the upper bowel are partially or completely neutralized by the acid chyme; consequently the digestion of fats and carbohydrates is still further delayed, while peptic digestion is impeded by the admixture of biliary salts. To counteract these ill effects, the harmonious glandular co-operation in the digestive act is called into activity by stimuli originating in the mucous membrane of the duodenum from the superacid chyme, which causes large volumes of pancreatic juice to be secreted.

(β) MOTOR DERANGEMENT of the intestine in the form of constipation is practically a constant symptom. The exact mode of production remains in doubt, but that the changes in the bacteriologic flora of the intestine, wrought by the thorough disinfection of the food by HCl, plays a role seems reasonable to suspect.

(3) THE SYSTEMIC EFFECTS of this functional perversion are *per se* not marked.

(α) THE NUTRITION is not reduced, and patients suffering from hyperchlorhydria do not create the impression as being very sick.

(β) CHANGES IN THE BODY FLUIDS result during the period of HCl secretion. Large quantities of NaCl being broken up in the glands of the stomach, the Cl combining with the H to enter the cavity of this viscus, while the Na is re-entering the blood to form alkaline phosphate. The excessive alkalinity of the plasma is, however, soon corrected by renal activity. The urinary water now holds in solution the excess of Na set free in the gastric mucosa, while the chlorides are actually diminished. Turbidity from precipitation of earthy phosphates in the slightly alkaline urine during the height of HCl secretion may become evident even to the patient.

2. **Diminished: Hypochlorhydria or Anachlorhydria.** (*a*) **Causes.**—The causes of a diminution in HCl secreted by the stomach are less often dependent upon (α) NERVOUS INFLUENCES. A *hypochlorhydria,* extending sometimes over long periods of time, analogous to the hyperchlorhydria already described, may occur unaccompanied by anatomic changes, but ordinarily such a reduction is transient in duration and is of *reflex origin.* From Pawlow's researches it is learned why the diseases of the mouth and perversions of appetite have such an effect. *In shock,* after sexual abuses and during psychic emotions the flow of HCl often stops as the result of central impulses. In the *early stages of achylia* gastrica the HCl may be completely absent without any demonstrable lesions. Hemmeter states that in the primary or idiopathic variety of this disease the absence of secretion is evident long before anatomic changes occur, and is possibly an inherited functional debility.

Certain *drugs* like morphine by acting on the motor mechanism inhibit secretory activity.

(β) ALTERATIONS IN GLANDULAR STRUCTURE are the usual cause of a partial or complete suppression of the HCl secretion. They may vary in a degree from the slight or even *doubtful changes* accompanying the acute infectious diseases like pneumonia, typhoid, and tuberculosis, to a *complete atrophy* of the gastric mucosa, such as is seen in atrophic gastritis, or in the more benign atrophy of achylia gastrica, in the end stage of chronic gastritis, and in extreme dilatation of the stomach, even when not due to malignant disease. *Amyloid and fatty changes* may render the gastric glands unfit for activity, and the action of caustics may destroy them completely.

In *carcinoma of the stomach* the gastric secretion, although often containing a large quantity of water, even early, is devoid of HCl and enzymes. When this change takes place before motor insufficiency occurs it cannot be attributed to interstitial changes, and because a like effect may result when even a small *cancer is located in distant viscera,* like the liver, uterus, and breast, it seems that products of cancer cells have a specific affinity for the stomach glands.

The general tendency to *atrophy in old age* does not spare the gastric glands, and by diminished secretions disturbing digestion the existing systemic state becomes augmented.

Transient changes, as seen in the acute and subacute forms of gastritis, lead to a reduction of HCl secretion, which lasts until there is recovery from the lesion.

(γ) CONSTITUTIONAL DISEASES through alterations in the blood plasma can cause the secretion of HCl to become diminished or suppressed. This is seen in pronounced cachectic states and anæmias especially of the pernicious type. In pernicious anæmia the anachlorhydria is such a constant symptom that oftentimes the question of cause and effect has been raised.

Because urea has been found excreted into the stomach in nephritis authors have failed to consider the systemic state, and attributed the failure to secrete to the irritative local effect of this substance.

(δ) AN APPARENT ANACHLORHYDRIA may result when the HCl is neutralized by excessive volumes of swallowed or stomach mucus, copious hemorrhage, or regurgitated duodenal contents.

(*b*) **Effects.**—The effects of a diminished quantity or complete absence of HCl are greatly modified by the *motor power of the stomach.*

(1) IN THE STOMACH (*a*) THE DIGESTIVE PROCESSES are markedly altered: (I) *Salivary digestion,* unless arrested by the products of acid fermentation, may continue throughout the entire time; (II) *Peptic digestion* does not occur; the pepsinogen, although rarely present in normal amounts, requiring the action of an acid to render it active. When organic acids are produced in sufficient amounts to substitute for the HCl, the peptic glands too have usually undergone degeneration.

The food remains longer in the stomach because automatic relaxation of the pyloric ring is dependent upon a certain transformation of the food, which, according to Cannon,[18] is dependent upon the HCl admixture.

Thus the diminution of the acid exerts a twofold deleterious effect: stagnating the ingesta, and allowing uninhibited saprophytic multiplication. If, however, the mainstay of this bacteriologic flora is not prolonged beyond the seventh hour, but is regularly passed on into the intestine, untoward effects are not manifested in the stomach.

In the heterogeneous flora that flourishes in stagnated contents sometimes specific organisms predominate, as the long, thin, rod-like, non-motile, non-spore-bearing, lactic-acid-producing, Gram-staining, Oppler-Boas bacillus in carcinoma and yeast cells and sarcinæ ventriculi in the benign forms of motor derangement. Practically without exception the organisms are acid or gas-producing.

(β) THE MOTOR POWER OF THE STOMACH is often reduced. The interstitial changes in the mucosa primarily present, or the consequence of secondary irritation by products of fermentation extending to the muscular coat, result in a functional debility and motor insufficiency.

A vicious cycle thus started may lead to dilatation entirely independent of pyloric constriction following the stagnation of food and gaseous distention.

It is only when such motor derangements are established that conscious digestive disturbances result. Of these (I) *belching of gas* or fluid is most frequent and is considered by Boas as characteristic of gastric motor derangement. The gas is either odorless or has an offensive sour smell and a disagreeable, rancid taste. Regurgitated sour food masses impart a burning and acrid sensation in the lower portion of the œsophagus (pyrosis or cardialgia) and an unpleasant taste in the mouth, which do not differ essentially from those experienced with hyperchlorhydria. A bitter taste may be due to peptones or admixture of bile; hence in practice chemical tests become necessary to determine the cause.

In the pharynx and mouth chronic catarrhal processes are induced which, extending to the tongue, give rise to a variable appearance, most pronounced in the thick furring associated with cancer of the stomach. The *fœtor ex ore* accompanying such changes results chiefly from foul gases exhaling from the œsophagus and stomach.

From defective perceptions of tastes and flavors necessarily following such oral changes, a secondary diminution of HCl secretion follows, and another vicious cycle becomes established.

(II) *Vomiting* is of rarer occurrence and is oftener dependent on the underlying cause, as an ulcerated carcinoma, irritating substances ingested, or constitutional state, and accidental events, such as hemorrhage or perigastritis, than upon local action of decomposition products. In the higher degrees of motor insufficiency it may become a means of periodically evacuating the stomach.

(III) *Variations in the pyloric ring,* if present, are often primary, and organic in character. Boas and Eichorst have attributed the pyloric insufficiency very rarely present in chronic gastritis to inflammatory infiltration of this musculature.

(γ) ABNORMAL SENSATIONS originating in the stomach in this secretory perversion, exclusive of those associated with the underlying cause, like carcinoma and gastritis, or accidental events, like motor insufficiency, are probably absent. Hemmeter speaking of achylia gastrica says: "The supposition of Biedert that there may be a great many who possess this defect and are unaware of it, has been verified by a number of observations among the students of my clinic."

But usually the dyspeptic disturbances are more marked, and a constant feeling of fulness and oppression after meals and even a vague painful sensation are complained of.

The appetite may be greatly diminished or perverted, while water is craved to satisfy the subjective sensations in the stomach. Nausea is at times present independent of vomiting.

(2) UPON THE INTESTINE falls the extra burden. In the classic experiment of Ludwig and Ogata it was emphatically proven that the intestine may vicariously assume the function of the stomach, and by observations of Martius and Lubarsch the results were substantiated, even clinically.

(*a*) THE SECRETIONS poured into the duodenum are diminished as the result of insufficient stimulation of the duodenal mucous membrane by a chyme of reduced acidity.

By experiments of Pawlow[20] it was shown that many organic acids, including lactic and butyric, could be substituted for the HCl in the chyme.

Intestinal digestion is thus chiefly modified by alterations in its bacteriologic flora; the augmented gaseous fermentation leading to tympanitic distention, while other decomposition products act as local irritants, and thus are explained the frequent diarrhœal attacks of some cases and the association of atrophic enteritis and atrophy of the gastric mucosa observed by Nothnagel.

Pathogenic germs like the typhoid bacillus, cholera vibrio, and dysentery bacillus, gain uninterrupted access to the intestinal tract, and various forms of lowly animal parasites like the trichomonas and cercomonas intestinalis are often found in the stools of those suffering from a long-continued anachlorhydria.

(*β*) VARIATIONS IN THE MOTOR FUNCTION are the rule. Usually constipation predominates and sometimes alternates with diarrhœa. The frequent diarrhœal attacks are in the main dependent upon decomposition products, formed either in the stomach or intestine; though the failure to properly disintegrate in the stomach, becomes a factor whenever mastication is hastily performed. Long-continued gaseous distention may result in ultimate paresis of the bowel.

(3) SYSTEMIC EFFECTS, although not well defined in the more benign forms of gastric atrophy, often become dangerous when motor defects predominate or malignant disease is the underlying cause.

(*a*) THE GENERAL NUTRITION remains good, while intestinal digestion compensates the lack of solution in the stomach, but when troublesome diarrhœa supervenes emaciation soon occurs.

A constant feeling of oppression, irritability of mind, and disinclination for bodily and mental exertion may from time to time be varied by more specific reflex and toxic visceral phenomena, such as headache, hypochondriasis, vertigo, dyspnœa, cardiac palpitation, myalgias, arthralgias, and insomnia. A depression of spirits may control the mentality and perversions of appetite oftentimes proceed to a disgust for ordinary diet.

(β) The Body Fluids are affected in various ways. (i) *The urine* fails to show the alkaline wave which follows the passage of Cl into the stomach at the height of digestion and often contains an excess of indoxyl and skatoxyl combinations which are formed from indol and skatol, the products of protein decomposition in the intestine. The normal proportion of conjugate or ethereal sulphates to preformed sulphates: 1:10 is increased, the ratio in intestinal putrefaction reaching as high as 1 : 8 or 1 : 5. Indican or potassium indoxyl sulphate is thus frequently detected in large amounts.

A characteristic odor of the freshly voided urine is often pronounced, especially when gaseous products or putrefaction predominates in the intestinal tract.

(ii) *The blood normally* carrying nutrition to even the remotest parts of the body may become impoverished, particularly in the extreme cases, where food, not digested in the stomach, is later hurried through an irritated or atrophied intestinal tube, where bacterial destruction predominates.

Much that has been said about the causal relationship of pernicious anæmia and absence of gastric secretion is summed up in the conclusions of Stockton,[21] viz.:

(i) In most cases of pernicious anæmia there is an absence of HCl secretion.

(ii) In most cases of achylia there is no pernicious anæmia.

(iii) In some cases of pernicious anæmia there is no achylia, but merely hypochlorhydria.

(iv) There is no improvement of the gastric secretion during the improvement of the anæmia.

The hyperleukocytosis accompanying normal digestion is less marked when the HCl is absent, and often fails to occur in cases of carcinoma.

b. The Enzymes.

Pepsinogen and rennin zymogen always secreted in parallel proportions, both in health and in disease, are much less subject to quantitative variations than the HCl.

1. **Increased.**—The amount of ferments secreted is increased in those cases where a continuous hypersecretion occurs as a symptom-complex, and often the digestive powers of the gastric juice are enhanced in cases of alimentary hyperchlorhydria.

That the secretion of enzymes is far less dependent on nervous influences is learned from the many cases of functional hypochlorhydria and anachlorhydria in which the ferments are found in normal amounts.

No ill-effects can result from hyperpepsia, the proteolysis proceeding rapidly, especially when the HCl is increased. When such a state prevails, pyloric relaxation must occur more frequently and the stomach empty itself in shorter lengths of time, but the reverse is often true, and results from the local effects of excessive quantities of HCl usually present.

2. **Diminished.**—Because the production of these enzymes is dependent on far less complex processes in the cell than the secretion of HCl, and is preceded by the deposition of proenzymes during periods of rest, while the HCl is formed only during periods of secretory activity by disruption of the sodium chloride molecule, it can be easily understood why the ferment secretory function is far more stable than the HCl-producing function.

Thus an immediate and proportionate reduction of ferments is not usually the accompaniment of the hypochlorhydria or anachlorhydria of neurotic origin, or of transient duration as in febrile disturbances—viz., influenza, typhoid, phthisis, and pneumonia—or dependent on reparable constitutional states, such as anæmia, exhaustion, renal insufficiency, and cardiac failure.

Shiff found that atropine, while causing a diminution in the gastric secretion, resulted in much greater reduction in the percentage of HCl than pepsin.

But in all atrophic and destructive lesions of the gastric mucosa the reduction of enzymes runs parallel with the extent of the process and in such chronic affections; when the filtrate obtained from the contents one hour after the ingestion of an Ewald test breakfast diluted 1:20, mixed with an equal volume of sweet milk, and kept at the incubator temperature for fifteen minutes, fails to solidly coagulate the mixture, it is assumed that incurable atrophy exists.

The effects upon peptic digestion vary with the cause and associated secretory and motor derangements. It becomes unnecessary to consider the consequences of suppressed rennin secretion in view of known physiologic facts, namely, the minor influence of this ferment, and that it cannot be diminished without a corresponding reduction of the pepsinogen.

But the influences of the hypochlorhydria, which is always associated with a reduction of ferments, are of the gravest importance because of the effects resulting from a diminution of HCl, *per se*, previously considered, and, secondly, that the proenzymes of these ferments secreted require an acid to change them into active pepsin and rennin. When the secretion of pepsinogen is not changed, and the optimum amounts of HCl are not available, proteolysis is impeded, but not arrested, as is seen in those cases where peptones are formed in the absence of free HCl. When anachlorhydria supervenes, organic acids, though rarely, may be substituted by fermentative processes for the HCl, but commonly apepsia soon results when such a degree of motor insufficiency develops.

c. Mucus.

This substance, secreted in small amounts normally by the mucosa of the pyloric portion, is subject more frequently to increased secretion.

1. **Increased Secretion.** (*a*) **Cause.**—*Increased secretion* occurs in all *catarrhal affections* of the stomach mucous membrane, so that clinically macroscopic quantities of mucus, intimately mixed with the contents, are taken as evidence of an existing gastritis.

In the alcoholic form large volumes of tenacious mucus are always secreted, and, together with swallowed pharyngeal and mouth secretions, accumulate during the night, to be vomited on arising—the so-called "*vomitus matutinus.*"

Of the numerous other forms of catarrhal gastritis, acute and chronic, due to *mechanical action,* as improperly masticated food, overeating, and ingestion of indigestible food, or *chemical irritation*—viz., excessive tea and coffee drinking, use of condiments, abuse of tobacco, habitual use of drugs and improperly prepared and spoiled foods, or *thermal influences,* like the irrational use of ice-water, hot drinks and food—should be mentioned also the *secondary varieties,* dependent upon *constitutional states* or *local diseases,* such as ectasy and atony, hypersecretion and hyperchlorhydria, carcinoma, ulcer and passive congestion.

In the *gastritis acida* of Boas the exact sequence of functional perversions still remains in doubt, it being claimed on the one hand that the inflammatory changes are provocative of the excessive HCl secretion, and on the other that the inflammatory changes are the result of the existing functional hyperchlorhydria with evidence in favor of the latter.

(*b*) **Effects.**—Because the gastric mucosa pours out large volumes of mucus whenever subjected to local irritations, it appears as if this were a means to counteract the ill effects by demulcent action, but practically another vicious cycle is thus started. (I) *Digestion* is interfered with in a purely mechanical manner by coating the food particles with a dense, tenacious layer, which is impermeable to the digestive fluids and chemically by neutralizing the HCl, which is often already reduced. By its alkaline reaction mucus in the stomach may prolong salivary digestion, but the beneficial results thus secured are always more than counterbalanced.

(II) *Nausea* is usually present when much mucus accumulates. In this way vomiting is induced and the stomach is emptied.

2. **Diminished Secretion.**—This is of rare occurrence, but is possible. (I) In the latest stages of all atrophic affections of the gastric mucous membrane. Usually mucus is still abundantly secreted after the HCl and ferments are completely absent; hence its value as a sign of gastritis. (II) In achylia gastrica, either with a

functional or anatomic substratum, the flow of gastric secretion is completely suppressed and mucus is absent.

d. Abnormal Constituents.

These may have a manifold origin, either (I) purely extraneous, as ingested ptomains, alcohol, and other drugs; or (II) from internal sources, such as the stomach itself, swallowed from the mouth, or regurgitated from the intestine.

1. **Extraneous Origin.**—The introduction of these substances does not have to be described and the possibilities need not be enumerated; while the effects of most drugs are considered in pharmacology, it seems best here to confine ourselves to the action of a few.

(*a*) **Alcohol** in small amounts of beer or light wine taken at the end of a meal may have a salutary effect upon digestion, especially if the subject has been accustomed to its use. The danger of inducing the habitual use of quantities that will cause serious inflammatory and degenerative changes in the stomach and other organs makes the prescription of alcoholic beverages for their possible tonic effect an unjustifiable hazard.

(*b*) **Alkalies.**—For a long time the effects of alkalies as promoters of the acid gastric secretion have been lauded, especially since the experiments of Claude Bernard; but since the Pawlow school has shown by more exact methods of research that secretion of HCl is not augmented by the introduction of alkali into the stomach, we can accept the statement of N. Reichmann "that sodium carbonate or bicarbonate does not act upon the secretory mechanism of the stomach, but only upon the juice already secreted, by neutralizing it and rendering the gastric contents alkaline."

The CO_2 thus liberated may cause annoying distention. The amounts of bicarbonate necessary may become excessive when compared with the magnesii usta (MgO), which has a four times greater binding power for HCl, while the salt thus formed has a later cathartic effect, which, according to Illoway, constitutes removing the cause of the hyperchlorhydria.

(*c*) **Acids.**—From a therapeutic viewpoint the introduction of acids often seems desirable (see Hypochlorhydria), but, as Ewald has pointed out, becomes difficult on account of the enormous quantities required. Let it be recalled that 100 gms. of milk require 0.3 to 0.5 gm. of pure HCl; of beef, mutton, pork, and ham, about 2 gms. of pure HCl, and potato and bread, from 0.3 to 0.5 gm. of pure HCl to saturate their protein affinities. (C. E. Simon.) Also that 0.37 gm. of pure HCl are contained in 10 c.c., or 150 gtts., of diluted HCl (U. S. P.).

The good effects usually obtained from even small doses can, on the basis of recent experiments, be attributed to the action of more highly acid chyme in the duodenum, and the more thorough disinfection of the food.

Cannon's demonstration of the effect of HCl in promoting automatic pyloric relaxation will help to throw light on the benefit derived from administration of small doses of HCl clinically in cases of hypochlorhydria.

(*d*) **Bitter Tonics and Stomachics.**—The various experimental and clinical results are harmonized and quickly summed up by the statement of Pawlow:[22] "It is the universal opinion of the earlier and later physicians that bitters increase the appetite, and if this be so everything is said. A person who suffers from digestive disturbances has, moreover, a blunted taste, a certain degree of gustatory indifference. The ordinary foods now appear tasteless. They not only arouse no desire for eating, but may even cause a feeling of dislike; there is no sense of taste, or, at the best, a perverse one. It is necessary, therefore, that the gustatory apparatus should receive a strong stimulus in order to restore a normal sensation. As experience teaches, this object is most quickly attained by exciting sharp, unpleasant gustatory impressions, which by contrast awaken the idea of pleasant ones, and here a physiologic law is illustrated. The light appears brighter after darkness, a sound louder after silence, and so on."

The action of some of the bitter tonics, as strychnine and alcohol, on the gastric musculature should not be lost sight of. Pawlow explains the action of bitters in the stomach by referring to the fact that certain impulses from the cavity of the stomach are necessary for the excitation of appetite, and thinks that bitters may also produce such impulses.

(*e*) **Antiseptics and Antizymotics,** such as carbolic acid and resorcin, β-naphthol, arsenous acid, volatile oils, and chloroform, are often administered to inhibit bacterial multiplication. The drug used must not be very irritant, nor very poisonous in the concentration required to disinfect the contents. For that reason it is necessary to cite only a few from the long lists of such remedies tabulated by Boer and von Langelsheim, Behring and Sternberg, and Micquel.

The bactericidal powers (killing anthrax bacilli in two hours) for alcohol is 1:10; for carbolic acid, 1:50; for creosote, 1:25, and for sodium arsenate, 1:250. The antiseptic or bacterial inhibiting power of course is much greater—*e. g.*, alcohol, 1:15: creosote, 1:250; eucalyptol, 1:150, and carbolic acid, 1:500.

It is further to be considered that excess of albumen can render many substances, especially the inorganic, inert; and that in strong solution these remedies become antizymotic—*i. e.*, interfering with the action of the enzymes.

2. **From Internal Sources.**—Such a contamination consists most commonly of abnormal secretions, excretions, or exudations derived from the stomach.

(*a*) **The Stomach.**—Either in the form of (*α*) DRUGS EXCRETED; of these morphine is most important. Repeated gastric lavage is necessary in intoxication by this alkaloid to remove from time to time the portions thus re-excreted. Morphine can be found in the stomach contents after hypodermic administration.

(*β*) PRODUCTS OF METABOLISM, such as urea in renal insufficiency, may contaminate the gastric juice. Fenwick states that the gastric mucosa is capable of excreting urea like the intestinal mucosa. Sugar has not been found in diabetes.

(*γ*) EXUDATION PRODUCTS, like the albuminous secretion of an ulcerated carcinoma or peptic ulcer, are sought for as a diagnostic sign. Salomon,[23] upon assuring himself that the stomach is empty after a twenty-four-hour fast, during which time a single meal free from albumen is given, which is followed in four hours by a lavage, washes out the stomach with 400 c.c. of water after a night's rest, and finds albumen containing at least 20 mgms. of N in 100 c.c. of wash water.

(*δ*) BLOOD is a frequent abnormal admixture of the stomach contents. Exclusive of that which has been swallowed, it is derived from erosion of large vessels, or by oozing from an ulcerated or abraded surface.

(I) *The causes which underlie gastric hemorrhage* can be classed as *systemic conditions*, such as *hemorrhagic diathesis*—viz., scurvy, purpura, hæmophilia, severe chronic anæmia, and jaundice. *Acute infectious diseases*—viz., yellow fever, smallpox and acute yellow atrophy of the liver. *Chronic nephritis* and *melæna neonatorum*, and *local causes*, such as *gastric ulcer*, where it occurs in 50 per cent. of all cases. *Malignant tumors* are the next most frequent cause. *Passive congestion*, either the result of heart and lung disease or from portal obstruction. Preble[24] was able to collect 60 fatal cases complicating hepatic cirrhosis. *Acute congestion* from intense acute inflammation or, rarely, a phenomenon of vicarious menstruation.

Traumatic, either the result of a direct injury and from foreign bodies, like a stomach-tube; or by violent acts of vomiting, as in pregnancy and seasickness. *Erosions of the gastric mucosa*, either caustic, thermal, or from hyperchlorhydria and hyperacidity.

Diseases of the gastric bloodvessels, as in gastritis, especially the toxic and chronic varieties, fatty and amyloid degeneration, or miliary aneurysms and varices. Also from a ruptured aneurysm or abscess of adjacent organs.

(II) *The effects of gastric hemorrhage*, when copious or oft repeated, may become general, resulting in an anæmia, which is dependent upon the amount of blood lost. The local manifestations are more often encountered. *Color variations*, from a bright red to a brownish-black, resembling coffee-grounds, depend upon the length of time the blood has remained in the stomach, the acidity of the contents, the rate of hemorrhage, and whether arterial or venous. Hence, the vomiting of bright-red blood, following the distention of the stomach, or occurring as a constitutional symptom of the resultant general anæmia, in ulcer of the stomach when large vessels become eroded, in contrast to the coffee-ground-like vomitus seen in carcinoma. The vomiting here is a symptom of motor insufficiency, while the blood gradually oozing from an ulcerated surface continually mixes with the stagnated acid contents and is turned black.

When the blood passes on into the intestines it always undergoes further changes, resulting in a tarry discoloration of the stools, but these decomposition products still give Almen's and Teichmann's blood tests, thus affording a means of recognizing even minute hemorrhages when blood is excluded from the diet.

Chemical effects, as the neutralizing of the stomach acids by the alkalies and albumins of the blood, render the digestion of large blood masses difficult. Absence of an appetite juice and the acute anæmia which necessarily results are important secondary factors in bringing about the acute indigestion and *vomiting* which often follows gastric hemorrhage.

Blood oozing from a thoracic aneurysm and entering the stomach through the œsophagus, or swallowed blood, may also be vomited; thus hæmatemesis and gastric hemorrhage are not synonymous terms.

(*b*) **Swallowed from the Mouth.**—From this source the abnormal salivary and buccal secretions and hemorrhage have already been considered. The effects of swallowed mucus do not differ essentially from mucus secreted in the stomach, except that the mechanical impediment to digestion cannot be so marked because of the incomplete admixture. Such mucus always occurs in larger masses, never intimately mixed with the contents, and upon microscopic examination is found to contain squamous epithelial cells from the mouth and dust-laden epithelial cells from the respiratory passages, both of which are entirely foreign to the stomach.

Bacteria, present in the mouth or entering it from adjoining cavities, like the nares, larynx, or trachea, frequently are swallowed, especially by children and semicomatose individuals. Of these the pneumococcus and tubercle bacillus, although often abundant, are rarely provocative of lesions, while Klebs-Loeffler bacilli may set up a diphtheritic gastritis. Swallowed leptothrices have been mistaken for Oppler-Boas bacilli.

(*c*) **Regurgitated from the Intestine.**—Resulting from the filling-up process or reversed peristalsis which occurs in intestinal obstruction, or by forcing back the duodenal contents through violent acts of vomiting or retching. Such accidents can occur while the stomach is full only when pyloric insufficiency results.

THE EFFECTS.—Although quite uniformly associated with arrested peptic digestion by the regurgitated alkalies, vary somewhat with the other abnormal constituents—*e. g.*, (I) *the Bile* checks peptic digestion by complete neutralization of the HCl, and deposits a resinous, flocculent precipitate of bile acids and syntonin.

The vomiting which occurs so frequently is usually the cause and not the effect of biliary regurgitation. Small quantities of bile do not interfere with gastric digestion. (Riegel.)

(II) *The Pancreatic Juice*, after neutralizing the HCl, becomes active and by means of its trypsin disintegrates the pepsin.

(III) *Fecal Material* from the lower intestine usually leads to rapid filling of the stomach, and emptying by acts of gulping and vomiting, which are more or less characteristic of the filling-up process. The vomitus is at first bile-stained and has a feculent odor, while later it becomes stercoraceous. The contents of the transverse colon may enter the stomach by a fistula, the result of carcinomatous ulceration.

(IV) *Intestinal Parasites*, like ascaris lumbricoides and hook-worms, may enter the stomach and be vomited, while the eggs of tænia solium can have their operculum digested, allowing the larval stage of the parasite to develop. These larvæ, subsequently deposited in the tissues and viscera, become encysted and are known as cysticerci cellulosa.

2. MOTOR DISTURBANCES.

a. Motor Insufficiency.

Motor insufficiency alone signifies a perversion of function in which the motor powers are insufficient. *Ectasy* means dilatation or permanent enlargement of the stomach combined with motor insufficiency.

A stomach abnormally large and distensible, without motor insufficiency, is known as a *megalogastria* and may occur as a congenital anomaly, but more commonly results from continuous overeating and excessive drinking; hence is seen in vegetarians and beer drinkers.

1. **The Causes.**—Certain conditions, either general or local, predispose to muscular atony. (*α*) Of the GENERAL FACTORS should be mentioned: (I) Anæmia and cachectic states; (II) excesses: sexual, tobacco, and alcohol; (III) sudden and violent emotions; (IV) narcotics, like alcohol, chloroform, and ether; (V) organic nervous disease, and (VI) hereditary weak stomach.

(*β*) THE LOCAL PREDISPOSING CONDITIONS ARE: (I) diseases of the gastric musculature—viz., carcinoma, chronic gastritis, toxic gastritis, traumatism, and cirrhosis of the stomach; (II) dislocations of the stomach, as gastroptosis, vertical position, and ventral hernia; (III) pyloric obstruction, either malignant (61 per cent. of gastric carcinomata involving the pylorus [Welch]) or benign. The benign causes of pyloric obstruction may be *intrinsic*, such as foreign bodies and polypi; *interstitial*, as pylorospasm, cicatrix from ulcer or toxic gastritis, hypertrophy of the pyloric musculature, either congenital or acquired after prolonged pylorospasm, and stenotic hypertrophic gastritis; and *extrinsic*, as peritoneal adhesions from cholecystitis or perigastritis, tumors of the pancreas and liver, and sometimes by traction from a floating kidney.

The Mode of Production gives rise to a classification—viz., (*a*) MOTOR INSUFFICIENCY may be (I) *Simple*—*i. e.*, a pure perversion of function resulting from a primary reduction of muscular power or when the quantity of material to be propelled is abnormally large. (II) *Relative.* Here an abnormal resistance is opposed to the exit of ingesta and a hypertrophic muscularis develops, which even by violent peristalsis is unable to pass the food through the stenosed orifice in the usual length of time.

(*β*) GASTRECTASIS.—This begins in the dependent parts, as along the greater curvature and fundus, and when due to pyloric stenosis may become extensive and lead to an ultimate atrophy of the muscularis.

The dilatation can occur as a (I) *Primary* process and be either *acute* following a traumatism or occurring postoperative, during acute infectious disease, or as a reflex disturbance in acute peritonitis, or *chronic.* This variety ultimately supervenes in cases of simple motor insufficiency. (II) *Secondary* ectasia results from pyloric stenosis, usually runs a chronic course, and is often preceded by a period of relative motor insufficiency.

2. **The Effects.**—Whenever insufficiency of the stomach musculature results, digestive disturbances develop immediately; thus the greater importance of good motility as compared even with the HCl secretion.

(*a*) THE MECHANICAL DISTURBANCES ARE: (I) *The stagnation of food*, varying from the retention of a few solid morsels beyond the seventh hour to almost a complete stasis in high degrees of pyloric constriction. (II) *The improper retention* of food by the sphincter antri pylorici in the various physiologic compartments of the stomach, thus allowing unrestrained mixture of the entire contents. (III) *Deficient mixture* of the food and gastric juice results especially when the movements of the pyloric portion are disturbed. (Cannon.[25]) (IV) *Fluids* which normally are held firmly in the grasp of the gastric muscle are now *unrestrained.* When under these conditions sudden pressure is brought to bear upon them and gas is present in sufficient amounts, a splashing sound is heard. (V) The constantly overweighted stomach may be subject to *downward displacement* (gastroptosis). This occurs rarely *in toto*, on account of the fixed cardiac end, but consists chiefly in a forcing down of the more movable pyloric portion. (VI) By constant distention *pressure effects* are brought to bear on adjoining viscera. The tympanitic distention of the abdomen which results is greatly aggravated by secondary gaseous fermentation in the intestine.

(β) THE CHEMICAL VARIATIONS resulting are dependent chiefly on the degree of mechanical disturbance, but are influenced by the underlying cause and the functional perversions of the gastric glands. Hypochlorhydria and excessive secretion of mucus producing the effects previously described. In carcinoma, excessive lactic acid fermentation, associated with a luxuriant growth of Oppler-Boas bacilli occurs very early, even before a high degree of motor insufficiency develops. Much smaller quantities of lactic acid are formed in pronounced cases of benign origin, and yeast cells and sarcinæ ventriculi are more apt to be present.

(1) *Saprophytic Infection.*—This results whenever the ingesta become *stagnated,* or are not *kept constantly in motion* by the churning movements of the stomach. *Decomposition products,* chiefly acids and gases, are formed in place of the normal products of digestion. The complexity of the substances thus formed can best be comprehended by considering the influences of various possible conditions, as the nature of the food, secretion of gastric juice, motility of the stomach and intestine, and the bacteria present in the stomach, mouth, and food.

Putrefaction and fermentation may occur simultaneously, and one or the other may predominate. Practically we recognize the products which predominate, and speak of lactic acid, acetic acid; alcoholic, gaseous, and hydrogen sulphide fermentation; while clinically, from the complex picture resulting from autointoxication, it is shown that many other substances are formed.

Abundant formation of lactic acid occurs when anachlorhydria exists with motor insufficiency. (Strauss.[26]) But, according to Hemmeter, the following conditions must also be fulfilled: absence of protein digestion, delayed absorption, and the presence of lactic acid bacilli. Lactic acid fermentation can be induced by a variety of micro-organisms, and only when accompanying carcinoma or following the atrophic gastritis in potassium poisoning (Schmidt[27]) is due to the Oppler-Boas bacillus. Here a complete anachlorhydria is always present.

Alcoholic fermentation can be carried on in either an alkaline or acid medium: $\frac{2}{10}$ per cent. HCl does not interfere seriously with the multiplication of the saccharomyces and sarcinæ ventriculi, while a $\frac{4}{10}$ per cent. solution is not entirely incompatible with the growth of these organisms. In hypochlorhydria, and even hyperchlorhydria with motor insufficiency, this form of fermentation is not an infrequent occurrence.

Gaseous fermentation very frequently observed is often combined with the formation of other products—as the CO_2 in alcoholic fermentation.

$C_6H_{12}O_6 + H_2O = 2C_2H_5OH + 2CO_2 + H_2O$, and is also associated with butyric acid production. $C_6H_{12}O_6 = C_4H_8O_2 + CO_2 + 2H_2$.

H_2S is sometimes encountered as a product of protein putrefaction.

Butyric and acetic acid formation depends, according to Boas, upon the same factors as the production of lactic acid.

(II) *Digestive Disturbances.*—These not infrequently precede the motor insufficiency as the result of diminished secretion. As soon as the tonicity of the gastric musculature is lost, *salivary digestion,* which in health is carried on in the food mass held in the fundus for several hours (Davy and Cannon), may be arrested much earlier. This appears especially in those cases where hyperacidity supervenes in the stomach.

Gastric Digestion is primarily interfered with, except in cases of relative motor insufficiency, by the insufficient mixing of the food and gastric juice. But far more important are the secondary effects resulting from saprophytic multiplication. Here irritating substances are formed from the foods to be digested, yes, even from the enzymes themselves, which induce inflammatory changes in the mucosa, resulting in a secondary diminution of secretion.

(γ) THE ANATOMICAL CHANGES.—These result from (I) *chemical* action of the abnormal acids, like the butyric, oxalic, formic, and other bacterial products which are formed. The inflammatory changes which are induced are not limited to the mucous membrane, but may extend to the muscular coat and lead to secondary weakening. (II) *The mechanical effects* of the *food mass* retained and gases liberated play an important role in continuing a dilatation once begun.

(δ) SENSORY DISTURBANCES.—(I) *Subjective phenomena* may be manifold, varying from a slight feeling of epigastric oppression, weight, and distention, to interference with excursions of the diaphragm, and palpitation, bradycardia, or even cardiac failure, especially when the heart is also diseased.

Pain is not marked unless cancer or ulcer is coexistent with the dilatation. When obstruction exists at the pylorus a feeling of unrest may follow the ingestion of food, which results from spasmodic movements of the hypertrophied musculature.

The appetite remains normal at the onset, while in advanced cases, where the stomach acts merely as a reservoir to retain the food until vomited, satiation results rapidly. In carcinoma anorexia and a distaste for meats is especially marked, even before a high degree of ectasia develops.

Thirst is always increased and becomes more pronounced with advancing dilatation. In some cases liquids by forming a softer pulp with the food mass may assist its passage through the pylorus. Water is not absorbed in the stomach.

Nausea is rarely a prominent symptom, except when large volumes of mucus accumulate, as in alcoholic gastritis, or from special decomposition products.

(II) *The objective symptoms* which depend on sensory impulses are *belching of gas and eructations*. These occur only when fermentation follows the stagnation of food, or when large volumes of air and gas are swallowed (aërophagia). Through the nervous mechanism the cardia becomes relaxed, and admits the regurgitation of accumulated gases and irritating foods. Contents thus escaping into the œsophagus, unless lifted into the mouth by the gas tension, remain in contact with its lower portion for variable lengths of time, and set up painful sensations (cardialgia) and burning (pyrosis). When reaching the pharynx (water brash) they lead to chronic inflammatory changes in the neighboring mucous membranes, which so often constitute a part of the clinical picture in gastric disorders. The gradually escaping gases and the oral condition result in a *fœtor ex ore*.

Vomiting is seen chiefly in the advanced cases of secondary gastrectasia. The attacks occur at irregular intervals and bear no relation to the stage of digestion. They occur suddenly and are rarely preceded by much nausea, it appearing as though the stomach were simply overflowing. When hypertrophy of the muscularis is present they may be preceded by cramp-like pains, and if hyperacidity is marked the vomiting seizure seems to occur as an attempt to relieve the condition.

Large quantities are vomited at one time, and often remains of food eaten a few days before are present in the vomitus. Pathologic admixtures have diagnostic significance—as the mucus in gastritis, coffee-ground-like altered blood in carcinoma, bright-red blood in ulcer, and bile in pyloric insufficiency or duodenal obstruction. Later when the dilatation becomes extreme, vomiting occurs less frequently and the putrefactive changes are more pronounced. The feeling of relief experienced becomes less and less.

(ε) THE CONSTITUTIONAL EFFECTS.—These are the consequences of malnutrition and autointoxication, which result from the disturbance of gastric and intestinal digestion.

(I) *The morbid processes* which underlie these changes begin in the *stomach*, where obnoxious substances are formed at the expense of the ingested nourishment. The amount of food which actually enters the intestine in some advanced cases, where either an extreme anorexia prevails or regular vomiting occurs, is greatly reduced, as is shown by the small amounts of feces passed. From 120 to 150 gms. of solid feces are passed normally, while in cases of advanced dilatation as low as 50 gms., on an average, are voided in twenty-four hours.

In the intestines the fermentative processes continue not only during the usual length of time required for the passage of food through this tube, but over prolonged periods on account of the intestinal atony.

Constipation is usually obstinate, but may be interrupted by diarrhœal attacks induced by the acid contents. During these attacks the food is hurried along, and while saprophytic action is cut short absorption is greatly impeded.

(II) *The Systemic Alterations.*—Exclusive of those which are dependent upon the cause of the motor derangement the *nutritional disturbances* are the most constant.

Emaciation progresses rapidly in the more advanced forms of ectasy, while in the milder degrees of motor insufficiency the general nutrition is not much altered. The caloric loss through bacterial multiplication and emesis cannot be made good by increased alimentation, unless carefully regulated. Thus the tissues of the body are called upon to meet the caloric requirements.

Nutrition is also affected by the deficient amount of water which is presented for absorption. Although thirst is a constant symptom in the higher grades of motor derangement, oliguria runs parallel with the degree of dilatation (Boas), and the feces contain 30 to 40 per cent. less water than in health. Let it be recalled that practically no water is absorbed from the stomach.

Kussmaul attributed the tetany sometimes observed to a dehydration of nerve tissue. Acetone in the urine points to carbohydrate starvation, and diminutions of urea and sodium chloride are also evidences of malnutrition.

Autointoxication may lead to a variable assemblage of symptoms, and a latent form is recognized by Bouchard.[28]

To decide whether it is due to anomalous gastric or intestinal fermentation introduces the subject of absorption in the stomach. Meltzer[41] left 200 mgms. of strychnine in the stomach of a dog with a ligated pylorus for many hours and failed to produce convulsions. Yet potassium iodide appears in the saliva in less than fifteen minutes after it is taken, but in the higher degrees of atrophy even its absorption is delayed sometimes for two hours.

Nervous symptoms usually predominate, such as headache, stupor, depression, disinclination for work, restlessness, and hypochondriasis. Vertigo is frequently complained of in advanced cases, and may take the form of an agoraphobia. Tetany is one of the more serious complications, and a form of coma may sometimes terminate the scene, especially in cancer. Kussmaul attributed these accidents to rapid absorption of toxic substances.

The *cardiopulmonary symptoms*, as the palpitation, asthmatic attacks, and cough, cannot always be attributed to purely mechanical effects. Arteriosclerosis can result from intestinal putrefaction.

A multitudinous variety of *cutaneous affections* are attributed to digestive disorders, such as urticaria, acne, eczema, and evanescent erythemas.

A curious relationship seems to exist between certain chronic deforming *arthritisms* and gastric disorders, as was shown clinically by Bouchard twenty years ago, and recently demonstrated chemically by Helen Baldwin[26] in Herter's laboratory.

In the urine combinations of the aromatic rings split from protein molecules during putrefactive processes occur, as ethereal or conjugate sulphates, of which indoxyl potassium sulphate (indican) is the most abundant. Sometimes the uric acid is increased; oxalic and volatile fatty acids may be present. Odoriferous gases may escape from the freshly voided urine in small amounts.

b. Pyloric Insufficiency.

1. **Causes.**—Incontinence of the pylorus, though of rare occurrence, is most commonly dependent on (I) *organic disease,* as inflammatory infiltration in acute and chronic gastritis, and more rarely to carcinomatous invasion. An atonicity of the pylorus may be associated with a chronic primary gastrectasia. (II) A *functional* relaxation may follow when extreme pressure is brought to bear, as in cases of intestinal or duodenal obstruction. Through nervous impulses a paralysis may occur in cases of myelitis and hysteria.

2. **Effects.**—Unrestrained passage of material, either one way or the other, can now occur: (I) *From the failure to retain the stomach contents until sufficiently disintegrated,* or attaining the usual transformation, larger food masses escape peptic digestion and in the intestine set up mechanical irritation. Favored by augmented intestinal motility the digestion of such morsels is rarely completed.

Gas formed in the stomach, swallowed, or introduced artificially, rapidly enters the intestine. Idiopathic tympanites, as seen in hysteria, may follow aërophagia in these cases.

(II) *By allowing free regurgitation of duodenal* contents, bile and pancreatic juice often enter the stomach. Bile can be obtained by lavage in these cases during times when the stomach should be empty. In intestinal obstruction of the usual type, the pyloric paralysis allows filling of the stomach by feculent material.

c. Insufficiency of the Cardia (Rumination).

Normally the tone of the cardiac sphincter is less than that of the pylorus, and when the stomach is overdistended with gas relaxation of the cardia results in belching.

1. **Causes.**—Cardiac relaxation is most commonly associated with motor insufficiency, and occurs when the stomach contents are ejected by emesis. An idiopathic form is seen in individuals with a certain nervous or hereditary predisposition. Psychic irritations and badly masticated food may bring on the attacks. Sometimes relaxation can be voluntarily induced.

2. **Results.**—When only gas and air escape (belching) but slight distress is experienced. Regurgitation of food masses gives rise to unpleasant sensations and are expectorated. Rumination, or merycism, is the term applied when ingesta that have risen to the mouth are immediately swallowed again.

The taste and local effects of the regurgitated material depend upon the stage of gastric digestion. An insufficient tone of the cardia may allow a continuous and gradual escape of gases, which result in the sour odor emanating from the mouth of those afflicted with gastric fermentation.

d. Hypermotility.

Hypermotility is the term applied to a simple acceleration of the motor function of the stomach, while "gastrospasm" and "peristaltic unrest" (Kussmaul)[30] are neuroses which may produce distressing symptoms.

1. **Causes.**—Hyperkineses or augmented motor activity of the stomach may result from: (I) *Chemical influences.* The excess of HCl in hypersecretion, hyperchlorhydria, and round ulcer usually leads to a rapid emptying of the stomach. Here the effects upon the pylorus are probably primary. (II) *Mechanical causes,* such as an obstructed pylorus or duodenum, lead to hyperperistalsis. (III) *To nervous influences* are attributed the idiopathic cases, especially those in which spasmodic activity results when the stomach is empty. In some cases of achylia gastrica rapid passage of the food into the intestine occurs.

2. **Effects.**—No ill-effects can occur from a hypermotility, *per se,* while distressing symptoms may develop in the cases where other functional perversions coexist or persistaltic restlessness results. Hypertrophy of the muscular coat follows excessive function.

Digestive disturbances are prone to develop when the food is passed rapidly into the intestine. They are dependent upon the imperfect transformation in the stomach, the effects of diminished acids on the flow of pancreatic secretion, the exposure of coarse food morsels to the intestinal fluids, and, lastly, upon the intestinal hypermotility which often prevails primarily or is induced.

e. Pylorospasm.

1. **Causes.**—Spasm of the pylorus occurs frequently: (I) *Chemical influences* are the usual cause, such as the excess of HCl seen in hyperchlorhydria, hypersecretion, and round ulcer. Organic acids rarely set up spasms. (II) *Mechanical effects explain* the tonic contraction of the pylorus which follows gaseous distention. Irritation by coarse food morsels always results in prompt contraction. (III) *Nervous influences* are a rare cause of primary pylorospasm.

2. **Effects.**—The effects of pylorospasm are twofold—viz., pain due to the cramp-like contraction, and pyloric obstruction with its consequences. Prolonged overactivity may lead to physiologic hypertrophy, thus rendering the stenosis more complete.

f. Spasm of the Cardia.

1. **Causes.**—The causes of cardiospasm are practically identical with those of spasm of the pylorus, except that nervous influences predominate. While the spasm may occur as a pure neurosis, it more frequently has a quasinervous substratum, as hysteria, neurasthenia, or even tetanus.

2. **Effects.**—The effects vary with the duration of the spasm. Disturbances of deglutition result, as in obstruction of the œsophagus. These usually set in abruptly and show a tendency to sudden remittance and recurrence.

The dilatation of the stomach, or so-called pneumotosis, seen in cases of air swallowing (aërophagia) is probably dependent to some extent upon a coexisting cardiospasm. Intragastric formation of gases may sometimes be similarly complicated.

g. Vomiting.

The nervous mechanism and description of this complex act having been considered in a previous chapter, we can willingly dispense with a further consideration at this point and proceed to enumerate the manifold causes.

1. **Causes.**—(1) *Through centric influences* vomiting may be induced. The rise of intracranial pressure which accompanies tumors, meningitis, and hemorrhage is such a force. The close proximity of the respiratory and vomiting centres explains the frequent association of vomiting and severe fits of coughing, as seen in whooping-cough.

Through toxic influences emesis may be produced. Various emetics like apomorphine, tartar emetic, ipecacuanha, senega, and squill; drugs like opium, chloroform, ether, alcohol, and nicotine, and sewer gases, act through the medullary centre.

The toxins of many specific infections like scarlatina, variola, acute pneumonia, and yellow fever have a similar effect.

Autointoxications, especially uræmia and cholæmia, or metabolic perversions like gout and diabetes may result in excitation of the vomiting centre. Hyperemesis gravidarum is doubtless often a true toxæmia.

Anæmia of the centre may lead to nausea and vomiting: in shock, syncope, and in severe acute or chronic general anæmia.

Through psychic influences vomiting is induced in hysteria and neurasthenia. Of even more obscure origin is the "periodic" vomitng of Leyden and the attacks of "juvenile vomiting" sometimes observed.

(II) *By Reflex Paths.*—Reflex vomiting is common and the influences initiating the attacks may proceed from the most distant viscera, specialized sensory end organs, or the stomach mucosa.

By silent impulses from the female generative organs like a pregnant or displaced uterus; or an uncorrected refractive error; or worms in the intestine, emesis may ensue. Painful impulses from all sources, especially the peritoneum, incarcerated hernia, spasmodically contracting bile-ducts and ureters, are, however, the most frequent cause.

But the most important region for such impulses is the stomach tself. Here chemical and mechanical means are equally potent. That vomiting is almost a constant symptom of acute gastric disorders and results normally whenever mild irritants, like warm salt-water, are brought in contact with the mucous membrane, while in chronic gastritis and motor insufficiency it fails to occur, is the result of a certain blunting of this sense which takes place in these gradually developing cases. Witness the comparative insensibility of the pharynx in atrophic pharyngitis to irritation otherwise provocative of nausea and reflex vomiting.

Also note the difference between the chronic overdistention of the stomach with high grades of dilatation and the filling of this viscus by regurgitation from intestinal obstruction. In the former instance emesis is long delayed, and, indeed, often invoked by the patient to give him relief of the increasing epigastric distress, while in the latter the gulping and vomiting attacks are often frequent and distressing, especially when compared with the sensory disturbances in the stomach.

Vomiting results more regularly in chronic gastric disorders where additional painful impulses supervene, originating either in the exposed surface of an ulcer or produced by carcinomatous invasion. The acute pain and reflex action following the administration of caustics and irritant emetics lead to prompt emesis.

Spinal impulses can produce distressing and painful vomiting attacks such as are seen in the gastric crisis of tabes. Similar attacks can occur in hysteria and with movable kidney, as Dietl's crises.

Painful affections of the central nervous system, like hemicrania, concussion, and meningitis, start impulses which stimulate the vomitng centre, while certain morbid visual and labyrinthine impressions, as in seasickness and Ménière's disease may also spread to this centre and set up nausea and vomiting.

2. **Effects.**—No generalization can state the effects of vomiting upon the organism.

(I) *Circulatory phenomena* accompany the act. Traube[31] was the irst to show that at the commencement of vomiting typical vagus pulsations occur, resulting in a lowering of the general arterial pressure. At the termination of the attack the pulse becomes accelerated and the arterial pressure rises even above the normal. This secondary rise of blood pressure, resulting when the vagus stimulation ceases, is dependent on the negative intrathoracic pressure which existed, and the influence of energetic muscular contractions. The cutaneous manifestations, as the initial paleness, which is followed by an exhilaration and free perspiration, are explained by the vascular changes.

(II) *Digestive alterations* are necessarily the most pronounced. Vomited material is definitely withdrawn from the organism. True enough, oftentimes irritating and obnoxious matter is gotten rid of in this way, thus sparing the stomach and the organism of its ill effects; but, on the contrary, the digestive tract may be unduly robbed of its contents, when the vomiting centre simply is irritated by local disturbances and circulating toxins, or wrongly interprets impulses from distant parts of the body.

(III) *Systemic effects,* in the form of inanition and its consequences, result when uncontrollable vomiting occurs, as is most often seen when a hypersensitive ulcer persists, or uncontrollable vomiting complicates pregnancy. Less graver disturbances result in some cases of persistent vomiting of neurotic origin.

The nutritional disturbances in chronic cases, although affecting all the body tissues, are most evident in the urine. Here a reduction in solid constituents, especially the urea and sodium chloride, are associated with an oliguria and excretion of acetone.

C. INTESTINAL DIGESTION.

1. THE SECRETIONS.

a. Diminished Pancreatic Juice.

1. **Causes.**—Diminutions of the external secretion of the pancreas can be caused by (I) *nervous influences;* doubtless these are a most frequent cause of *transient* alterations in the amount of pancreatic secretion. The morbid impulses arising either in the mouth, where perversions of appetite are dependent upon a stomatitis, in the stomach, where abnormal stasis of ingesta occurs, or from the surface of the duodenal mucosa, where a chyme, the product of pathologic gastric digestion, acts as an insufficient or morbid stimulus.

(II) *Alterations in the gland parenchyma* are here, as elsewhere, provocative of functional incapacity. Of inflammatory conditions it shares its quota. Two extreme grades are the most important clinically—viz., the chronic interstitial variety, commonly accompanied by glycosuria, on account of the involvement of the islands of Langerhans, and acute hemorrhagic pancreatitis, often rapidly fatal, and, according to Opie,[32] resulting in many cases from diversion of the bile into the pancreatic duct by biliary calculus impaction. Cysts, hemorrhages, and abscesses can completely destroy the gland.

Carcinomatous invasion, either as a primary lesion or secondary to gastric cancer, is not infrequent. Hyaline degeneration, tuberculous and syphilitic disease, and atrophy of old age are processes which may slowly destroy the glandular tissue, while in some acute infections the pancreas is the seat of fatty degeneration.

(III) *Duct obstruction*, either from calculus impaction or anatomic lesion, can deprive the intestine completely of the pancreatic juice. In some cases where the obstruction is located near the papillæ of Vater, the flow can be re-established if the duct of Wirsung has remained patent.

(IV) *The loss of body fluids* affects the pancreas in a manner quite analogous to the salivary glands. In febrile diseases of prolonged duration, as typhoid, this must become a significant factor.

2. **Effects.**—"Symptoms which follow impairment of the digestive or external function of the pancreas have not been very clearly defined and, though certain facts have been established, clinical observations are often divergent." (Opie.[33]) The fact must be emphasized that rarely disturbances in the digestion and assimilation of fat, muscle, and carbohydrates are observed clinically in acute pancreatic affection, but are almost invariably present in the more extensive and protracted disorders.

(*a*) **Digestive Disturbances.**—The results observed by Claude Bernard,[35] Abelmann,[36] and others, after the total or partial extirpation of the pancreas in dogs, are more or less completely reproduced in the human subject when a deficiency or absence of the external pancreatic secretion is present.

(*α*) PROTEIN DIGESTION must consequently be interfered with. Abelmann found in his experiments on dogs that albuminous substances, which normally are absorbed except 1 or 2 per cent., were only absorbed to the extent of 44 per cent. after a total extirpation. When pigs' pancreas was given with the food, about 75 per cent. of the nitrogenous material ingested was absorbed.

Fles was the first to observe a similar condition clinically in cases of diabetes. He found numerous well-preserved muscle fibres in the stools, which disappeared when calves' pancreas was fed daily to the patient, and reappeared promptly when this treatment was omitted.

According to Schmidt,[34] the presence of undigested muscle fibres alone never indicates gastric indigestion, and only when found with elastic fibres mean an association of intestinal and gastric digestive disorders.

The work of Pawlow has shown why tryptic proteolysis can be inhibited by intestinal secretory insufficiency. That the time element is always an important factor in enzyme action is a well-established chemical fact.

Hence, faulty digestion and absorption of albumen (azotorrhœa) can result from a variety of gastric and intestinal disorders, but occurs especially in conditions of deficient secretion of enterokinase, and hypermotility of the small bowel, resulting from inflammatory processes or systemic conditions.

Delayed absorption, resulting from anatomic lesions of the intestinal mucosa or rapid transit of the contents, plays an important secondary role.

Thus azotorrhœa as a symptom of pancreatic disease loses its pathognomonic dignity.

(β) Starch Digestion, which normally is only started by the salivary secretion, depends largely upon the amylopsin for its completion in the intestine. Thus, the presence of well-defined, free starch granules in the stools are significant of intestinal indigestion. They mean a deficiency of pancreatic secretion only in the absence of other disturbing factors, such as an enteritis or diarrhœa hurrying on the intestinal contents, especially of the small bowel.

(γ) Fatty Stools (Steatorrhœa).—Here again the thorough experiments of Abelmann,[36] under the guidance of Minkowski, show results similar to those seen clinically. After total extirpation he found that non-emulsified fats were not at all absorbed, and, when emulsified, only to an extent of 18.5 per cent. When fats were given in the form of large amounts of milk, about 30 per cent. of the fat was absorbed. The administration of pigs' pancreas facilitated the absorption of fat in these cases.

Clinically, Kuntzmann,[37] in 1820, was the first to associate fatty stools and disease of the pancreas. The many and variable observations since his time are classed by Oser under the three following headings: (I) Diseases of the pancreas, showing fatty stools. These are quite numerous and, of course, easily explained. (II) Disease of the pancreas without fatty stools. A number of such cases are reported, and Müller, basing his conclusions chiefly upon these observations, concludes that a free flow of bile can replace the action of the lipase, and doubts whether steatorrhœa can be a symptom of uncomplicated pancreatic disease. Abelmann assumes that in these cases a portion of secretory gland parenchyma remains, or in cases of common duct obstruction that secondary communication is established with the bowel by way of a patent duct of Wirsung. (III) Fatty stools without alterations of the pancreas. These can follow the ingestion of abnormally large quantities of fat or from the delayed absorption, dependent upon anatomic changes either in the intestinal mucosa, such as inflammatory processes, atrophy, and amyloid degeneration, or in the mesenteric lymphatic vessels and glands. Steatorrhœa promptly follows the exclusion of bile from the intestine. In this condition pancreatic enzyme activity is necessarily inhibited. (Pawlow.)

(*b*) **Systemic Effects.**—These can result from the (*α*) NUTRITIONAL DISTURBANCES which must follow the chronic derangements of intestinal digestion, especially when complicated by gastric disorders.

In cases where sclerosis of the islands of Langerhans exists, as in interacinar lesions complicating the changes in the secretory gland parenchyma, the metabolism of the diminished quantity of absorbable carbohydrates formed is further interfered with, and sugar and acetone may be found in the urine, especially in chronic cases.

(*β*) AUTOINTOXICATION can result where excessive intestinal putrefaction and fermentation prevails at the expense of protein and carbohydrate contents which, from lack of enzymes, remain unabsorbable. But clinically the symptoms (*γ*) DEPENDING UPON THE UNDERLYING CAUSE usually predominate. This is observed especially in cases of acute hemorrhagic pancreatitis, where shock and toxæmia often lead to a fatal termination before digestive disturbances are recognized.

The cachexia associated with carcinoma and the jaundice following common-duct obstruction can completely overshadow the secretory incapacity.

Reflex salivation may complicate pancreatic disease.

(*δ*) FAT NECROSIS deserves mention as a frequent accidental occurrence. This results when the lipolytic ferment of the pancreas comes in contact with living fat tissue. The fat molecule is split up into fatty acid and glycerin. By combining with the circulating calcium the fatty acid is laid down in the form of a calcium soap; while the glycerin and lipase are absorbed to be excreted in the urine, where, by chemical tests, they can often be recognized, thus aiding in the diagnosis of this impalpable intra-abdominal condition. (Robson and Cammidge.[39])

The foci of necrotic fat are most abundant in the immediate neighborhood of the pancreas, but may be widely disseminated. They are not raised above the surface of the neighboring adipose tissue, have an opaque homogeneous appearance, and are yellowish-white in color.

b. The Bile: Diminished Secretion.

The amount of bile normally secreted is subject to wide quantitative variations, and alterations in composition of this fluid are almost hourly occurrences as the consequence of metabolic fluctuations.

Abnormal admixtures can result as the consequence *of hepatic disease.* Brauer[40] found coagulable albumin in the bile in parenchymatous hepatic affections. A false albuminocholia can result in diseases of the biliary passages. Rokitansky,[42] Haupt,[43] and others found structures resembling urinary casts in these conditions, while Brauer found these biliary casts in animals after the ingestion of large doses of alcohol.

Substances accumulated in the blood can, to some extent, pass into the bile like urea in renal insufficiency, sugar in diabetes; also some drugs like methylene blue, sodium salicylate, copper salts, and potassium iodide.

Because an *increased quantity* of bile poured into the intestine can do no harm by augmenting the digestive and absorptive processes, and at the most lead to moderate hypermotility of the small bowel, with its consequences, we can limit our discussion to the effects of *diminished secretion of bile and acholia* upon digestion.

1. **Causes.**—Considering the complex mechanism concerned in the production of bile, the causes resulting in a diminution may be classified as: (α) ALTERATIONS IN THE GLAND SUBSTANCE. It is self-evident that *destruction of gland parenchyma* renders bile production impossible; hence almost a complete cessation of secretion can occur in such diseases as acute yellow atrophy and inflammatory necrosis. A reduction results when partial destruction of hepatic tissue occurs, as in cirrhosis, brown atrophy, purulent affections, destruction by multiple tumors, and in fatty and amyloid degenerations.

(β) LOWERING OF BLOOD PRESSURE, as in passive congestion from cardiac insufficiency, or capillary paresis resulting from cord lesions, causes a reduction of secretion.

(γ) LOSS OF BODY FLUIDS AND ALTERATIONS in the constitution of the BLOOD are not infrequent causes of diminished bile secretion. General blood concentration, either the result of anæmia or an accompaniment of febrile disorders, exerts the usual effects, and the resulting reduction is often aggravated by coexisting parenchymatous alterations.

Doubtless the quality and quantity of the portal blood is often a determining factor, as portal-vein obstruction leads to a prompt reduction of biliary secretion. The drugs causing a diminished secretion cannot be accurately enumerated, except that opium causes a reduction of all body secretions except the sweat, and that atropine affects the bile like the other secretions.

(δ) DISTURBANCES IN THE NERVOUS MECHANISM, according to the observations of Pawlow, must be an important factor. Clinically the origin of simulating impulses in the form of peptic proteolytes and ingesta rich in fat are recognizable, while their course remains in darkness.

(ε) BILIARY-DUCT OBSTRUCTION is the most frequent and important cause of impediment or divergence of the bile stream. The causes which can produce an occlusion may be classed as: (1) *Intrinsic,* h as gallstones; catarrhal inflammation; thick, viscid bile; hemorge, polypi, and parasites entering either from the intestine or the r. (II) *Interstitial*, as cicatricial contraction, congenital atresia, smodic stricture, and neoplasms, either carcinoma or adenoma.) *Extrinsic*, such as tumors of the liver, pylorus, pancreas, and ney; enlarged glands at the porta hepatis; aneurysm of the atic artery; constriction from chronic perihepatitis and perichogitis, and slit-like narrowing by traction from movable kidney or eroptosis.

The obstruction may occur in the larger biliary passages, at the denal orifice, from a gastroduodenitis, impacted pancreatic culus, and intestinal obstruction; or in the finer bile capillaries, ere the secretion pressure is lowest, by viscid bile or mucoid terial.

. **Effects.**—(*a*) THE SYSTEMIC EFFECTS of acholia are the maniations of perverted metabolism and are considered in that pter.

β) THE DISTURBANCES OF INTESTINAL DIGESTION depend upon threefold action of the bile, viz.:

I) *Inhibition of peptic digestion* in the duodenum by neutralizing gastric acidities is essential for pancreatic digestion.

When this is not affected by the secretion of bile, the acid chyme ning with the slightly alkaline pancreatic juice results in a mixture acid reaction. This reaction being foreign to the jejunal mucosa en induces hypermotility, and, being unfavorable for pancreatic zyme activity, may result in their destruction through peptic prolysis.

This affected peptic digestion is also arrested by accumulated cus entericus or bacterial activity, and an inert mixture results.

II) *As an auxiliary of pancreatic digestion* (Pawlow) the influences an acholia are exerted chiefly on the fatty constituents of the diet. nce, lipolysis becomes practically arrested, and the absorption of , unaided by the saponifying and osmotic tension reducing propies of the biliary fluid, reaches a minimum.

III) *Aiding absorption, especially of fats.* Hence the explanation of atorrhœa or fatty stools in these cases. According to F. Müller[44] m 55.2 to 78.5 per cent. of all ingested fat was passed in the es when the bile was completely excluded from the intestine; ereas under normal conditions from 6.9 to 10.5 per cent. was cuated.

The large amount of fat is not alone responsible for the clay color these stools. Normally the biliary pigments undergo marked erations and are practically reabsorbed in the intestinal tract, so t the normal feces fail to give tests for bilirubin and biliverdin. t enough altered bile pigment always remains, chiefly in the form robilin (stercobilin), to give a distinct color in health.

(iv) *Stimulating peristalsis* is a secondary function of the bile. In the absence of biliary secretion constipation is not always a consequence, because other factors provocative of intestinal peristalsis are brought into play, like the effects of acid on the small bowel, previously mentioned, and increased bacterial multiplication at the expense of the undigested foodstuffs throughout the intestinal tube.

The stools in these conditions often have an offensive or rancid odor, and gases may be passed freely from the bowel.

(v) *The antiseptic properties* of the bile are doubtless overrated. Chiari[45] and Fütterer were the first to show that many organisms, including the typhoid bacillus, can live for many months in the gall-bladder. The intestinal fermentation resulting in the absence of bile can easily be explained on other bases.

c. The Succus Entericus.

N. B.

This fluid normally poured out in large volumes throughout the intestinal tract is doubtless very frequently changed in quantity and altered in composition. Since Pawlow's demonstration of the auxiliary ferment enterokinase in this secretion, the quantitative fluctuations have become most significant, and, if it were possible to recognize them by clinical methods, probably many intestinal indigestions would be explained.

1. **Increased Secretion.**—Cohnheim thought that the rice-water dejecta of cholera resulted from hypersecretion by Brunner's and Lieberkühn's glands, because he could not explain the amylolytic properties of these stools by simple exudation processes. But because the cholera vibrio grows luxuriantly on potato it may have amylolytic properties, and, secondly, the rapid transit of the pancreatic juice through the intestinal tube favors the preservation of the amylopsin.

The increased secretion associated with watery diarrhœas, without anatomic alterations, can be attributed to simple functional perversions. As the ill effects of such a variation result only from the increased quantities of water poured into the intestine, they need no special description. Kühne[46] demonstrated that pilocarpine caused a copious flow of intestinal secretion.

2. **Diminished Secretion** is of more frequent occurrence.

(*a*) THE CAUSES, although not well defined, are surely numerous. (i) Anatomic changes in the intestinal mucosa, such as acute and chronic inflammations, primary and secondary atrophic processes, can destroy or incapacitate the intestinal glands. (ii) The nervous influences concerned may also be at fault. It has been thought that such derangement prevails in some cases of chronic constipation. (iii) Systemic alteration doubtless often are the underlying cause of quantitative variations.

(β) THE EFFECTS are the result of (I) *diminished secretion of liquid* into the intestinal tube, from which constipation may result. Herter thinks that probably often diminished secretion of succus entericus and diminished motility develop simultaneously. (II) Due to the absence of enterokinase, the proteolytic properties of the pancreatic secretion are greatly inhibited. Following this disturbed protein digestion, excessive putrefaction may be induced, especially within the large bowel, and the excretion of nitrogen in the dejecta may be increased.

Not enough is known of the invertin to recognize clinically the effects resulting when it is insufficient.

(γ) ALTERATIONS IN COMPOSITION can occur when toxic substances like morphine, iodides, bromides, and mercury bichloride are secreted into the intestine. In uræmia the accumulated katabolites, like urea, and poisonous products may be eliminated through the intestinal mucosa. The persistent watery diarrhœa often seen in these cases results in part from the irritating effects of these substances *per se* and derived decomposition products, like ammonium carbonate from urea. A vicarious mode of elimination is thus established, compensating in part the renal insufficiency.

d. Mucus.

Normally small amounts of mucus are secreted throughout the intestinal tube, and chemical tests for this substance in the feces are always obtainable. No digestive disturbances can result from a reduction of this practically inert substance, and if slight alterations should occur they could not be separately distinguished from the underlying atrophic processes.

Increased secretion always leads to the appearance of macroscopic quantities in the excreta.

1. Causes.—(I) *Catarrhal inflammations* of the intestinal mucous membrane always are associated with excessive excretion of mucus. When large volumes of stomach mucus pass on into the intestine a similar condition results, but nevertheless the admixture of mucus in the excreta retains its diagnostic significance.

(II) *Through nervous disturbances* the secretion of mucus can be excited. It is claimed that in some cases of mucous colitis associated with hysteria and neurasthenia no anatomic changes are demonstrable in the colon.

(III) *Considerable accumulations* of steady secretion from even the healthy bowel can result when it is not removed by regular evacuations. (Nothnagel.)

2. Effects.—Here again, as in the stomach, the mucous membrane reacts to irritation by pouring out this alkaline fluid, thus diluting noxious substances or counteracting their local effects by demulcent properties.

Both digestion and absorption are delayed by the presence of mucus, chiefly in a mechanical way. The food particles are coated by a thin layer of viscid mucus, and are thus rendered impermeable to the intestinal fluids. That colloidal substances retard absorption is established pharmacologically when the slow absorption of opium is compared with morphine.

The abnormal admixture of mucus becomes most apparent in the dejecta. The appearance varies with the location in the intestinal tube where this occurs. If mucus is poured out freely by the small intestine or first portion of the colon, it becomes thoroughly mixed with the liquid contents at this point, and imparts to the voided feces a uniform, pasty consistency. Microscopic masses may become bile-stained.

When the mucus enters the remainder of the colon and rectum it comes in contact with more solid contents which it cannot permeate, hence is deposited as a thick, glairy layer on the surface. In mucous colic a periodical voluminous evacuation of mucus, aggregated in ribbon-shaped shreds or membranous masses, occurs. Pure, thick, glistening mucus mixed with feces is sometimes voided in diseased conditions of the rectum or lower portion of the sigmoid.

2. MOTOR DISTURBANCES.

a. Diarrhœa (Hypermotility).

Transudation and exudation into the intestine and hypermotility are so closely associated that no attempt will be made to consider them separately.

1. **Causes.**—Because the exact physiologic processes are so variable, and in many instances doubtless multiple, the causes of diarrhœa can be classed as follows:

(*a*) **Predisposing Factors:**

I. Body States:
- (α) *Age;* infants; children and aged.
- (β) *Hereditary predisposition* and neurotic temperaments.
- (γ) *Constitutional Diseases.*
  - (i) Acute infectious diseases. Toxic influences.
  - (ii) Chronic. Heart, lung, or liver diseases; passive congestion.
  - (iii) Bright's disease.
  - (iv) Cachectic conditions. Cancer, anæmia, etc.
  - (v) Extensive cutaneous burns.
  - (vi) Neuroses.

(δ) *Local Conditions*:
- (I) Diseases of the stomach.
- (II) Passive congestion.
- (III) Disorders of canalization.
- (IV) Neighboring disease processes. Peritonitis, cancer.
- (V) Abnormalities of position. Hernia, enteroptosis.
- (VI) Altered secretion. Bile, pancreatic juice.
- (VII) Sluggishness of the bowels and atony.
- (VIII) Other diseases of the bowel—*e. g.*, *ulceration* and carcinoma.

II. ENVIRONMENT:
- (α) *Residence.* Tropics.
- (β) *Season.* Summer.
- (γ) *Occupation.* Requiring exposure.

(*b*) **Exciting Cause:**

I. TOXIC. (Toxic catarrhal enteritis.)
- (α) *Introduced directly:*
  - (I) Corrosive alkalies. Acid, salts of heavy metals, metaloids, etc.
  - (II) Alcohol and volatile oils, turpentine.
  - (III) Carbolic and other aromatic acids.
  - (IV) Vegetable cathartics: croton oil, colchicum.
  - (V) Spices: mustard, pepper.
- (β) *Contained in the food:* decomposed food, meat, sausage, fish, etc. (Tyrotoxin, lactotoxin, muscarin, cadaverin, etc.)
- (γ) *In the blood* circulating through the intestinal wall. Uræmia, mercurial poisoning, extensive cutaneous burns.

II. INFECTIVE. (Infective catarrhal enteritis.)
- (α) *Intestinal infection* as a symptom of a general infection.
  - (I) Acute. Typhoid, cholera, sepsis, influenza, pneumonia.
  - (II) Chronic. Tuberculosis.
- (β) *Microbic action* limited to the intestine.
  - (I) Indirectly: decomposing intestinal contents and producing chemical irritants.
    - (*aa*) Action of the ordinary intestinal bacteria.
    - (*bb*) More specific organisms, as in some forms of summer diarrhœa.
  - (II) Directly:
    - (*aa*) Summer diarrhœa of infants.
    - (*bb*) Æstivo-epidemic diarrhœas.

III. Thermal:
- (i) Changes of weather.
- (ii) Exposure to cold (catching cold).
- (iii) Excessive heat of the summer (diarrhœal diseases of children).
- (iv) Cold articles of food and drink (ice-cream).

IV. Mechanical:
- (i) Overeating.
- (ii) Traumatism (to abdomen).
- (iii) Foreign bodies, swallowed; gallstones; enteroliths.
- (iv) Intestinal parasites, especially tape-worm and ascaris lumbricoides.
- (v) Coprostasis.

V. Parasitic:
- (α) *Infusoria:*
  - (i) Cercomonas intestinalis.
  - (ii) Trichomonas intestinalis.
  - (iii) Megastoma entericum.
- (β) *Ascaris lumbricoides* (round-worm).
- (γ) *Ankylostoma duodenale* (hook-worm).
- (δ) *Trichocephalus dispar* (whip-worm).
- (ε) *Cestodes* (tape-worm).

VI. Nervous:
- (i) Transient emotions.
- (ii) Dentition (?).
- (iii) Exophthalmic goitre.

1. **Effects.**—The deleterious influences of copious liquid evacuations must necessarily result in grave local and general disturbances, but in some instances may be actually beneficial on account of the noxious substances gotten rid of. (*a*) Derangements of digestion are largely dependent upon the segment of the bowel affected. (i) The *small intestine* can be involved alone. In these cases digestive disturbances result from the time restrictions to pancreatic digestion. Hence meat fibres and starch granules are found in the dejecta, which are now bile-stained from a failure to properly disintegrate the biliary pigments in their rapid transit through the intestinal canal. The feces are usually acid in reaction, and, if the diarrhœa is a manifestation of enteritis, apparent mucus is found intimately admixed. No liquid evacuations need occur. (ii) *When the colon* is alone involved, the absorptive function is chiefly interfered with. The well-digested contents of the small intestine are hurried along, with no time for absorption of favorably altered foodstuffs. The absorption of water is greatly impeded, and copious liquid dejecta are the consequence.

h the nitrogen excretion may not fall below that resulting permotility of the small bowel, unaltered bile, pancreatic ıd undigested muscle fibres and starch granules are not , unless the small intestine is simultaneously involved.

NSORY DISTURBANCES resulting from hypermotility are re- iefly to the causes. *Intestinal colic* does not result from simple l peristalsis, but is associated with spasm of the muscularis, ıay be symptomatic of organic disease or occur as a pure urosis. *As a neurosis* it occurs chiefly in anæmic, neuras- or hypochondriac persons. Reflexly it may result from to cold and after traumatisms. Intestinal crises of locomotor re of spinal origin. Colicky contractions can also be invoked irritation of worms, indigestible food masses, enteroliths, ated gases, and by toxic agents like lead and tyrotoxicon pon the nerve endings in the intestine. *Organic lesions* ıce spasmodic contractions, especially when interfering with sit of the contents, as in intestinal obstruction, appendicitis, nteritis, and the like.

NSTITUTIONAL EFFECTS are the disturbances of *nutrition*, which om the derangements of the digestion and absorption in the . The loss of water or the prolonged hypermotility of the comes an important factor and results not only in apparent and diminished general glandular activity, but also in grave ic disturbances.

effects are often greatly varied by predisposing and exciting

b. Constipation.

icient motor powers of the intestine need not necessarily lead ıulations in the large bowel only, but may invite fermentative s in the small intestine, where favorable media for bacterial ation is most abundant, which when exerting their influences olon can actually augment its motility.

inal contents can also be retained by spastic contraction of n hindering their passage; thus it becomes evident that tion is not always significant of intestinal atony.

uses.—According to Nothnagel and Illoway, constipation can om the following conditions:

Perversion of Certain Functions which still remain physiologic.

α) Qualitative and quantitative *changes in the food*, considering idiosyncrasies.

β) *Diminished fluids:*

  (I) Small quantity ingested.

  (II) Excessive quantity lost by skin.

γ) *Deficient muscular exercise.*

(*b*) **As a Result of a Pathologic State** or as a symptom of an abnormal condition.

- (*a*) *Diseases of the stomach:*
  - (I) Ulcer and hyperchlorhydria.
  - (II) Chronic gastritis and carcinoma.
  - (III) Pyloric stenosis and dilatation.
- (*β*) *Diseases of the intestine:*
  - (I) Chronic enteritis—colitis.
  - (II) Enteroptosis.
- (*γ*) *Diseases of the pancreas and liver:*
  - (I) Bile diminished or absent.
  - (II) Portal congestion.
- (*δ*) *Certain acute febrile diseases.* Sometimes alternating w[illegible] diarrhœa—*e. g.*, typhoid.
- (*ε*) *Malformations:*
  - (I) Undue size or length of sigmoid.
  - (II) Abnormally developed or atrophic colon.
  - (III) Diaphragms in the rectum.
- (*ϛ*) *Painful diseases of the rectum*, inducing voluntary abste[illegible]tion from stool; piles, fissure, ulcer, etc.

(*c*) **Sluggishness of the Bowels** as an independent patholog[illegible] entity. (Habitual constipation.)

- (*a*) *Atonic variety.* Simple weakness of the intestine.
- (*β*) *Spastic form.* Retention of fecal masses within segment[illegible] of spastically contracted intestine.
- (*γ*) *Fragmentary form.* (Boas) Evacuations incomplete; sluggishness of the rectum.

2. **Effects.**—Stasis of intestinal contents, especially when rich in foodstuffs, invites excessive bacterial activity, the products of which remain within the most active absorbing surface of the body. The manifestations of such processes depend greatly upon their location, and secondarily are subjected to both quantitative and qualitative variations by such factors as constituents of diet, functional capacity of the stomach, state of intestinal digestion and absorption, nervous stability of the patient, and activity of emunctory organs.

(*a*) **Local Disturbances.**—Fecal accumulations in the colon, especially in its lower portion, are associated with infrequent evacuations of inspissated dejecta (constipation); while frequent watery movements can result from sluggishness of the small bowel, in a manner previously described. The result being so essentially different, it can be taken for granted that the underlying processes are not alike.

(I) *In the colon* absorptive processes predominate. The foodstuffs undergoing the ultimate digestive changes as the cæcum is being approached, and also being gradually absorbed in their transit, are normally much less abundant in the colon; hence furnish less nourishment for saprophytic multiplication. The rapid absorption of water throughout the large intestine tends also to produce an unfavorable bacterial media, especially when extended through longer periods of time.

Such processes naturally reach their climax in the rectum and sigmoid. Here the desiccation often becomes marked, so that the inspissated contents can act as mechanical irritants to the mucosa, in response to which a hypersecretion of mucus results, with which they become enveloped. This mucous coating impedes absorptive processes and may also aid in the ultimate passage.

The accumulation of these hard masses results in obstruction to the return flow of blood through the hemorrhoidal veins, following which there occurs a dilatation of the radicals of the hemorrhoidal plexus. Depending upon the location of these varices, either beneath the rectal mucous membrane or at the anal orifice, they are classed as internal or external hemorrhoids.

The passage of these fecal accumulations is influenced by the tone of the rectal musculature. When spasticity prevails, as is found chiefly in neurasthenics, hypochondriacs, and women with pelvic disorders, the stools, according to Fleiner,[47] assume the shape of long or short cylinders of small calibre, often no thicker than a lead-pencil, or spherical masses the size of hazelnuts.

In the usual form of constipation, where atonicity is present, the stools are drier and firmer than usual, and consist of compressed and desiccated lumps or cylinders of large calibre, or of distinct particles or scybalæ bearing the impress of sacculations of the colon.

Boas was the first to recognize fragmentary evacuations, resulting probably from the sluggishness of the lower segments of the large intestine. Here the call to defecation follows the passage of small quantities of feces into the lower rectal segments, while the retention in the higher portions gives the sensation of fulness which, while at stool, leads to great straining and later causes renewed attempts, during which fragmentary masses are only expelled.

If defecation becomes habitually insufficient larger accumulations, called fecal tumors when palpable, may result. These may set up secondary inflammation and even start diarrhœal attacks.

A feeling of distention and discomfort in the abdomen may occur. Abdominal developments of flatus or spasmodic colicky contractions of the colonic musculature are among accidental results.

(II) *In the small intestine* conditions even normally are favorable for rapid bacterial growth, which, when extended over longer periods of time by sluggish motility, can assume the most luxuriant proportions. Because such a condition cannot produce constipation *per se*, but may ultimately supervene in cases of fecal accumulation, it deserves but passing mention at this point and will be considered under Ileus.

(*b*) **The Systemic Effects** in constipation are much more dependent on the underlying cause than the resultant digestive disturbances.

The statement that increased quantities of ethereal sulphates, including indican, are not found in the urine in simple constipation, verified by such authorities as Jaffe,[48] Nothnagel,[49] and C. E. Simon,[50] is not hard to explain. Putrefactive processes must necessarily be at a minimum in the desiccated food remnants, and absorption of toxic substances is certainly greatly hampered by the envelope of thick mucus. Hence, the constitutional disturbances are not marked unless the mild autointoxication finds a victim in an irritable nervous system, or an hereditary weak arterial tree.

When the prolonged accumulation of feces in the rectum leads to a moderate degree of relative obstruction a slight autointoxication may result, with symptoms varying from a feeling of pressure, heaviness, and stupor in the head, to a violent headache, moderate vertigo, and a feeling of heat in the head. The relationship between constipation, hyperchlorhydria, and chlorosis, so frequently observed clinically, remains in doubt.

In those cases where a gastric disorder is primary, such as motor insufficiency and hyperchlorhydria, or where intestinal obstruction or atony supervene in fecal impaction, the digestive and systemic disorders are all modified by the secondary processes.

c. Ileus.

Ileus is a symptom-complex due to many causes characterized clinically by pain, nausea and vomiting, tympanites and coprostasis. Treves defines *intestinal obstruction* as including a great variety of conditions, which, although unlike in character, have yet the common property of bringing about mechanically an obstruction to the passage of matter along the intestine.

1. **Causes.**—The numerous causes through which the symptom-complex of ileus may arise, according to Murphy, Treves, and others, can best be tabulated as follows:

I. **Paralysis of the Bowel (Adynamic Ileus).**

- (*a*) Functional Nervous Paralysis of the Intestine.
  - (*α*) *Of the afferent nerve.*
    - (I) Spinal lesions.
    - (II) Afferent nerve lesions, as trauma to the mesentery.
  - (*β*) *Reflexly by stimulation of the inhibitory nerve.*
    - (I) Strangulated omentum.
    - (II) Biliary colic.
    - (III) Renal colic.
    - (IV) Ovarian compression.
    - (V) Diaphragmatic pleurisy in pneumonia.

(*b*) MARKED ANATOMIC LESIONS OF THE INTESTINE.
  (I) Prolonged strangulation.
  (II) Embolism of mesenteric artery.
  (III) Atonicity, seen in some cases of chronic constipation.

(*c*) TOXIC ENTEROPARALYSIS.
  (*α*) *Septic.*
    (I) Local peritonitis.
    (II) General peritonitis
    (III) Thrombophlebitis.
  (*β*) *Uræmic.*

Spasm of the Bowel (**Dynamic Ileus**).
  (*α*) *Specific toxic effect of lead* to produce spasm of the intestinal muscularis. This can be counteracted by morphine, which has a peripheral action, and leads to paralysis of Auerbach's plexus. (Sollmann.)
  (*β*) *Tyrotoxicon poisoning.*

I. **Mechanical Obstruction** (**Mechanical Ileus**).

(*a*) INTRINSIC CAUSES.
  (I) Foreign bodies: gallstones, enteroliths.
  (II) Fecal impaction.

(*b*) INTERSTITIAL CAUSES.
  (*α*) *Malignant or benign neoplasms.*
  (*β*) *Cicatricial contractures* (*strictures*).
    (I) Tuberculous or syphilitic ulcers.
    (II) Traumatic wounds.
    (III) Carcinoma.
  (*γ*) *Intussusception.*

(*c*) EXTRINSIC CAUSES.
  (*α*) *Compression by tumors.*
  (*β*) *Strangulations by bands and apertures.*
  (*γ*) *Incarcerations.*
    (I) External hernial apertures.
    (II) Internal apertures or under bands.
  (*δ*) *Volvulus.*

Effects.—(*a*) **The Local Distubances** are primary and the most ninent. Of these (*α*) COPROSTASIS, which may be absolute dynamic ileus and acute strangulation or only partial in dynamic and partial obstruction, is the most important.

) *Fecal accumulation* occurs above the point of obstruction; this *vomiting* results. The vomiting may at first be reflex, but occurs as the consequence of the filling up processes not only accumulated ingesta, but also from the exudation which takes e into the bowel. That actual reversed peristalsis occurs is denied by many surgeons. Later it may continue as a reflex phenomenon of a secondary peritonitis. The character of the vomitus varies with the location of the lesion and time after the accident. At first it is gastric, then bilious, then feculent, later may even become stercoraceous. It is usually persistent and copious.

When the seat of obstruction is in the duodenum or jejunum, vomiting occurs early, is persistent, and always bile-stained. It is much influenced by food, and never really becomes stercoraceous. In obstructions involving the middle of the ileum the vomitus really never becomes stercoraceous, unless long retained with opium.

When the lower ileum or colon becomes obstructed, vomiting occurs more irregularly, is more commonly stercoraceous, but later may be scanty and comparatively slight.

Meteorism results also at first from a filling-up process, as there is no exit for the normal intestinal gases. Gaseous fermentation of the stagnated contents soon augments the primary condition. In paralytic ileus the greater distensibility of the intestinal coils seems to allow more free expansion of the gaseous contents. The degree depends on the completeness of the occlusion, but also upon the location of the lesion and tonicity of the bowel. It is more marked and earliest when the colon is obstructed, especially in volvulus.

In obstruction of the small bowel, the median parts of the abdomen become distended, while in occlusions of the colon the distention is more general, but most marked over the colon.

It is not much reduced by vomiting and diarrhœa, but may be slightly lessened by strychnine and morphine.

(II) *Increased fermentation* is a most important consequence. The stasis favors bacterial multiplication in any portion of the intestinal tract, but especially in the small intestine, where nutrient material is most abundant. Putrefaction and fermentation usually occur together. In the less acute forms carbohydrate fermentation may excel and precede albuminous putrefaction; hence, often in these cases, unless a diet rich in proteins is taken, the ethereal sulphates in the urine may not be much increased.

The products of fermentation are cyclic compounds and H_2S split from the protein molecules, fatty acids, CO_2, H_2 and other gases derived from carbohydrates, and even higher fatty acids resulting from cleavage of fat molecules. Indicanuria is a constant accompaniment of ileus, providing, of course, that protein substances are present for decomposition. In obstruction of the small intestine and reflex ileus associated with general peritonitis it appears in one to two days, while in obstruction of the large intestine this symptom may be delayed for three to five days.

In the sluggishness of the bowel resulting by reflex impulses from slight peritoneal irritation in appendicitis and salpingitis, I have always found the indican in the urine slightly increased.

The portion of bowel below the obstruction is empty (obstipation), completely when the occlusion is perfect, or partially when incomplete obstruction is present. Sometimes a spurious diarrhœa develops from the accumulation of exudation products and hemorrhage, especially in intussusception.

(β) PAIN, variable in degree and duration, *occurs* early *from* the damage to the bowel, later from distention and futile peristalses, and finally as a symptom of secondary peritonitis.

The *mode of onset* depends upon the suddenness of the strangulation, the amount of bowel involved, and other circumstances, like peritonitis, carcinoma, etc.

Its *location* is variable; either diffuse or most marked in the navel region, and sometimes is definitely localized over the lesion. It is variable in degree; often severe early, and later less, due to collapse. Exciting peristalsis, as by taking of food, use of enemata, and rectal examination aggravates the pain. Early it is not associated with tenderness; often it is even benefited by pressure; but later, when peritoneal irritation occurs, tenderness is marked. With approaching collapse the perception of tenderness is less acute.

The *course* varies with the degree of occlusion when obstruction is complete; it is constant with slight periodic exacerbation, while in partial obstruction it tends to be more intermittent with intervals free from pain.

(γ) THE INTESTINAL PERISTALSIS varies with the cause. (I) *In dynamic ileus* the bowel, especially the colon, is spastically contracted. (II) *In adynamic ileus* peristalsis is arrested either in segments or throughout the entire tract. *In mechanical ileus* the effects differ essentially with the duration of the process. In an *acute attack*, violent non-visible peristalsis occurs, with colicky, spasmodic pains. An attempt is made to overcome the obstruction, and often results in the forcing through of gases in partial obstruction with a rumbling sound (borborygmus). Hypertrophy does not result in so short a time. In complete obstruction the hyperperistalsis rarely occurs and an atonic condition soon supervenes.

In more chronic cases violent, visible peristalsis results from the hypertrophy of the muscularis that develops to compensate the lesion. This is often most marked or limited to the region of the lesion. The peristaltic movements are accompanied by colicky pains. Atonicity may supervene when the obstruction becomes complete.

(*b*) **The Systemic Effects** are pronounced, both in the acute and chronic cases. Gradual exhaustion results from the continuous pain and vomiting, the inability to take food, and from autointoxication.

The primary cause, like a malignant tumor or peritonitis, greatly influence the course, while *complications*, like perforation, peritonitis, and inhalation pneumonia, may terminate the scene.

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CHAPTER VI.

ABSORPTION: INTRODUCTION.

ABSORPTION DEFINED.
STRUCTURES INVOLVED IN ABSORPTION.
PHYSICAL FORCES INFLUENCING ABSORPTION.
FORMER THEORIES OF ABSORPTION, REVIEWED.

THE PHYSIOLOGY OF ABSORPTION.

ABSORPTION FROM DIFFERENT PORTIONS OF THE ALIMENTARY CANAL.
- *a.* ABSORPTION FROM THE MOUTH.
- *b* ABSORPTION FROM THE STOMACH.
- *c.* ABSORPTION FROM THE SMALL INTESTINE.
- *d.* ABSORPTION FROM THE LARGE INTESTINE.

ABSORPTION OF DIFFERENT FOODSTUFFS.
- *a.* THE ABSORPTION OF WATER.
- *b.* THE ABSORPTION OF SALTS.
- *c.* THE ABSORPTION OF CARBOHYDRATES.
- *d.* THE ABSORPTION OF PROTEINS.
- *e.* THE ABSORPTION OF FATS.

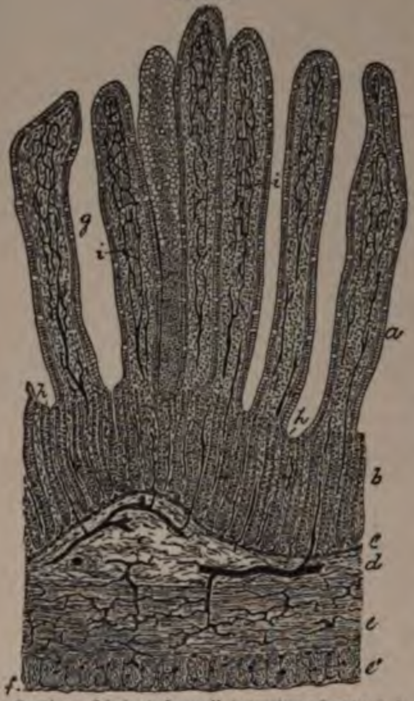
ABSORPTION.

INTRODUCTION.

1. ABSORPTION DEFINED.

THE term *absorption* in its general sense means imbibition, and lies with special fitness to the "*drinking in*" of a liquid by any ous body, such as a sponge. In this sense it is a purely physical cess, depending upon the *capillary attraction* exerted by the illary pores of the body upon the liquid. This term has been ended to include such processes as the taking in of water by minating seeds, a purely physical process depending upon the s of diffusion or osmosis. It was the most natural thing to extend term to the process by which an organism takes up food from medium in which it exists, or from canals in which foods have n dissolved or otherwise prepared. *Absorption*, then, *is that ction of the organism through the exercise of which the system* *takes in nutriment through a boundary epithelium.* It has been thought that the absorption by the system of the products of digestion is a purely physical process, depending upon the interaction of two or three factors—osmosis, filtration.

FIG. 188



Section of injected small intestine of cat: *a*, *b*, mucosa; *g*, villi; *i*, their absorbent vessels; *h*, simple follicles; *c*, muscularis mucosæ; *d*, submucosa; *e*, *e'*, circular and longitudinal layers of muscle; *f*, fibrous coat. All the dark lines represent bloodvessels filled with the injection mass. (Piersol.)

Whether or not physical forces alone are sufficient to account for the phenomena of absorption will be discussed later. In the definition of absorption reference was made to the "boundary epithelium." The boundary epithelia of the mammalian body are: (I) the epithelium of the alimentary canal; (II) epithelium of the lung passages; (III) the epithelium of the urinary tract; (IV) the cuticle.

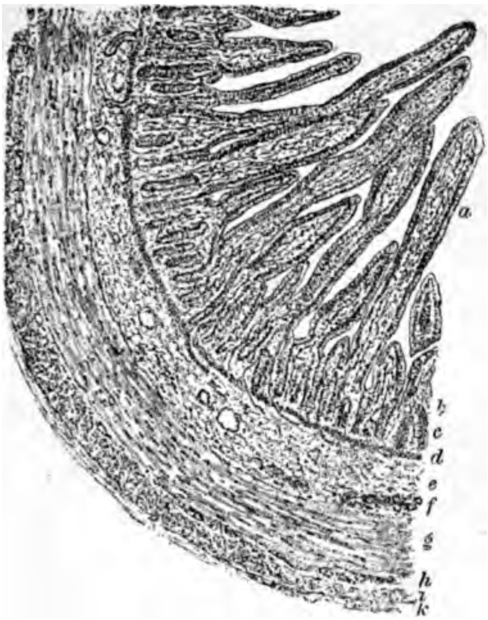
Of these boundaries the first is pre-eminently an absorptive surface, while the second is equally absorptive and excretory; the third is wholly excretory, and the fourth is practically non-absorptive, and its excretory and secretory functions are secondary to its especial function—protection.

It will be understood, from the expression "*boundary epithelium*," that the physiologist looks upon the contents of the alimentary canal, lung passages, and renal passages as being *really outside of the organism, though enclosed by the body*. What is in the alimentary canal is really not yet within the organism. When it passes within the outer boundary of the outer layer of cells, then it is within the organism, and the passage from the alimentary canal into the epithelial cells which surround this canal constitutes *absorption*.

2. STRUCTURES INVOLVED IN ABSORPTION.

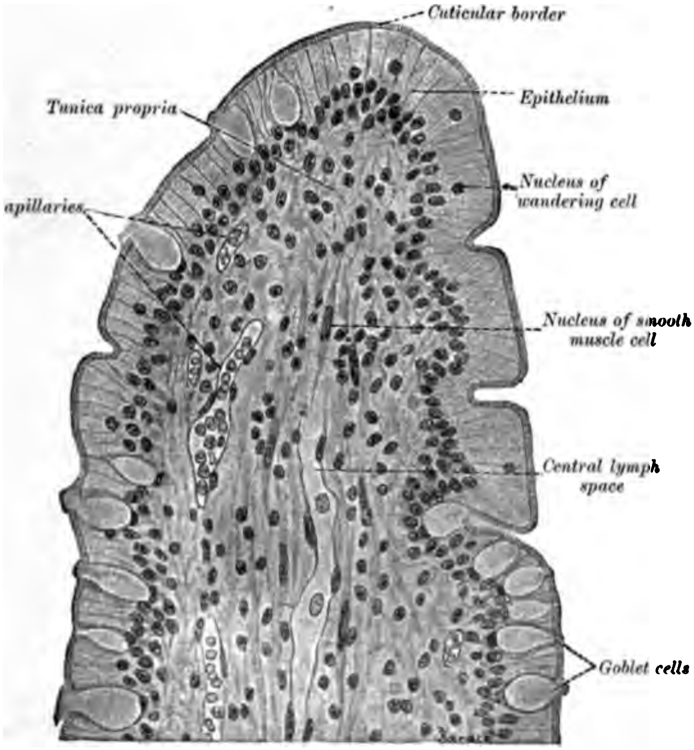
Whatever forces may be involved in the process of absorption—whether physical, mechanical, or vital—the area of absorbing surface must be an important factor in the total amount absorbed.

FIG. 189



Showing the frequent inequality of the villi. (Benda.)

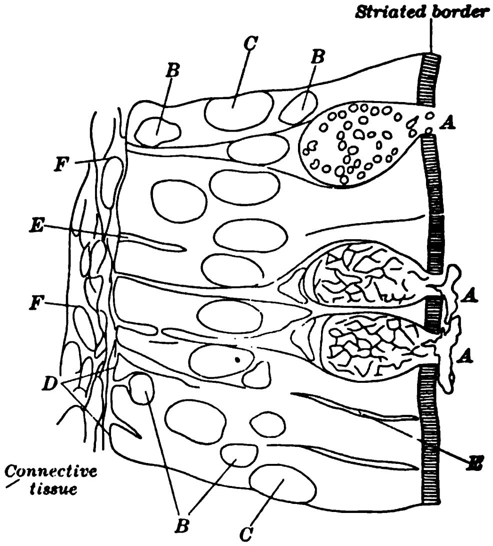
FIG. 190



Cross-section of an intestinal villus. (Szymonowicz.)

Under *Digestion, Introduction*, mention was made of the prominent transverse folds of the mucosa of the small intestine. These *valvulæ conniventes* make the mucous surface about three times as great as a straight cylindric lining of the same canal would be. Upon this folded mucous surface the microscope reveals innumerable, minute, finger-like projections—the villi. These projections are subcylindric in form, and the axis of the cylinder may be taken as averaging about

FIG. 191

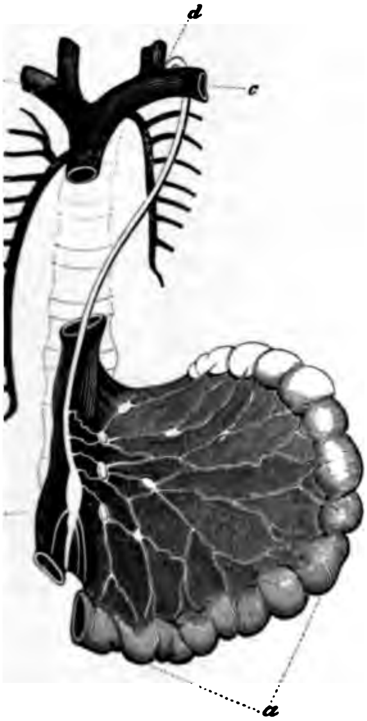


A = *Goblet cells*
B = *Wandering cells*
C = *Nuclei of epithelial cells*
D = *Basal membrane*
E = *Intercellular spaces*
F = *Cells of the reticular connective tissue*
(Szymonowicz.)

eight times the radius of the base. The area of the villus would then be about sixteen times as great as the area of the base, or the area of the whole surface occupied by villi is multiplied approximately sixteen times through the means of the villi. Thus the area of the epithelial surface is many times as great as the area of the intestine when considered as a smooth cylinder.

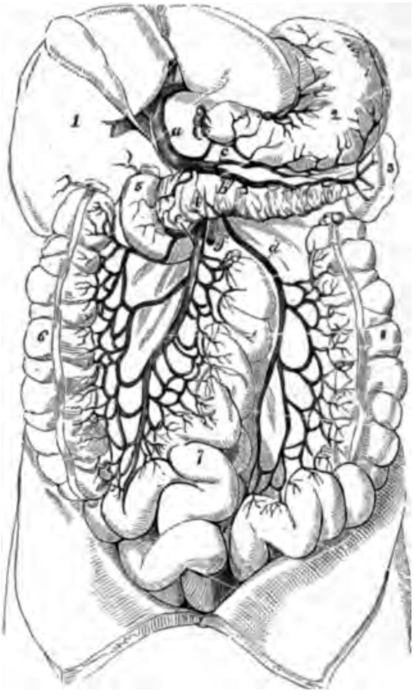
The accompanying figures show the structure and grouping of the villi. Note in Fig. 188 the coats of the intestine; the injected rteries and capillaries; the lymph radical in the second and fifth villi om the left; the ends of the cells shown in the third villus from the ft. Fig. 189 shows the marked inequality frequently to be noted the length of the villi. In Fig. 190 the minute structure of the lus is shown. Note, especially, the numerous capillaries which lie

FIG. 192



acteals, thoracic duct, etc.: *a*, intestine;
ena cava inferior; *c*, *c*, right and left sub-
vian veins; *d*, point of opening of thoracic
t into left subclavian. (Dalton.)

FIG. 193



View of the principal branches of the vena portæ. ⅙. 1, lower surface of the right lobe of the liver; 2, stomach; 3, spleen; 4, pancreas; 5, duodenum; 6, ascending colon; 7, small intestine; 8, descending colon; *a*, vena portæ, dividing in the transverse fissure of the liver; *b*, splenic vein; *c*, right gastroepiploic; *d*, inferior mesenteric; *e*, superior mesenteric vein; *f*, superior mesenteric artery. (Quain.)

st beneath the basement membrane; the muscle fibres, and the rge "central lacteal" or lymph radical.

In the intestine of such animals as the cat, rat, and rabbit the nger villi reach well toward the middle of the intestine.

The two courses which absorbed material takes are: (1) through e lacteals and thoracic duct to the venous system (see Fig. 192);) through the vena portæ to the liver (see Fig. 193).

3. PHYSICAL FORCES INFLUENCING ABSORPTION.

Just how far physical forces enter into the act of absorption has been a subject of controversy for a long time. Recent investigations tend to minimize the importance of the physical forces and to magnify that of the more distinctly physiological factor "selection." The student is, however, unable to understand the literature of the subject without at least a general knowledge of *Osmosis* and *Filtration*.

a. Osmosis.

The term osmosis is applied to diffusion taking place through a membrane. But diffusion involves a mutual or reciprocal interchange of space or a mutual interpenetration independent of any mechanical mixture or chemical reaction.

Let the open end of a large glass tube have an animal membrane stretched across it and fixed in place; let the tube be partly filled with a solution of any crystalline substance easily soluble in water, and let this dialyzer or endosometer be lowered into a jar or beaker of distilled water until the liquid within the dialyzer stands on the same level as that outside. These conditions fulfilled, one will observe, after a few hours, that the liquid within is higher than that in the beaker outside, making it evident that water has passed through the membrane into the distilled water. The raising of the liquid in the dialyzer above the level of that outside involves a certain amount of energy. This energy is measurable, and may be determined with a mercury manometer or by simply calculating the weight of the column of water supported by the pressure. This is called endosmotic pressure or osmotic pressure.

The osmotic pressure of a solution is a measure of the osmotic activity. The laws of osmotic pressure take into consideration only temperature, degree of concentration, and the influence of mixtures; but most important factors are the character of the membrane and of the solvent.

Summing up this brief discussion of osmosis one may give the following factors as concerned in the rate of osmosis:

(I) The quantitative composition of the solutions separated by the membrane, and consequently the partial osmotic pressure exerted by the several constituents.

(II) The coefficients of diffusion of the various constituents.

(III) The character of the membrane.

(IV) The character of the solvent.

(V) The temperature.

(VI) The hydrostatic pressure upon the two sides of the membrane (filtration).

b. Filtration.

Filtration is the passage of a liquid through a membrane under the influence of pressure. It is a purely mechanical process. In the animal body any filtration which may occur is complicated with an osmosis which is going on at the same time, for in every case the relation of liquid, membrane, and filtrate are such as have just been described under osmosis.

In fact, factor (VI) above gives *hydrostatic pressure* as one of the variables, so that in the living organism cases of filtration may be classified as cases of osmosis where the principal determining factor is *hydrostatic pressure.*

The following factors are active in filtration:

(I) The porosity of the membrane.
(II) The degree of pressure.
(III) The character of the liquid to be filtered.
(IV) The temperature of the liquid.
(V) The action of the liquid upon the membrane.
(VI) The osmotic relations of liquid to filtrate.

4. FORMER THEORIES OF ABSORPTION REVIEWED.

a. The Vital Energy Theory.

The earlier theories of the physiologists regarding the forces involved in absorption are very well represented by Tiedemann and Gmelin,[1] who likened it to *secretion,* and conceived that it was practically the same process *reversed* in *direction;* he ascribed to the cell the force necessary to accomplish this work, and looked upon it as one of the manifestations of the vital energy of the cell.

b. The Physical Theory.

The next generation of physiologists experienced a reaction against the vital-energy theory. The physical phenomena of diffusion, osmosis, and imbibition were better understood. Ludwig, Brücke, and their associates were devoting their energies toward the solution of physiologic problems through the laws of chemistry, physics, and mechanics. These efforts had a most salutary effect upon physiology. That field of human knowledge assumed under these men the dignity of an experimental science. The methods of investigation were the exact methods of the chemical or physical laboratory.

It was the hope of this school of physiologists to account for all of the phenomena of life as the manifestation of the action, and more or less complex interaction, of the forces already known in chemistry and physics. They considered that the processes of digestion are chemical processes, pure and simple; that *the processes of absorption are physical and mechanical processes, pure and simple.*

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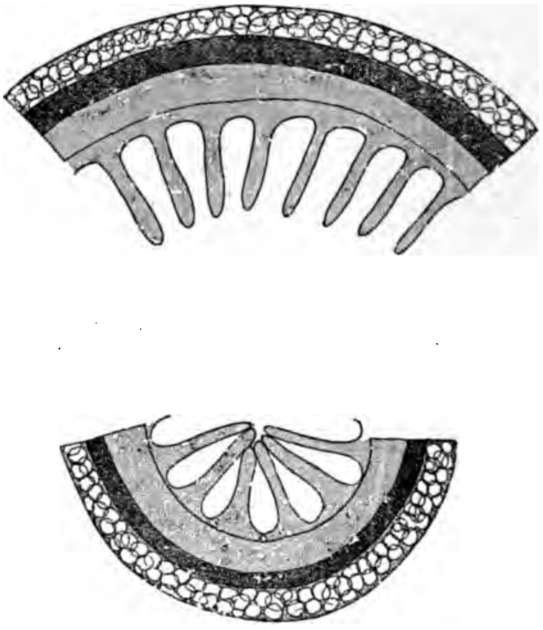
[1] Quoted by Heidenhain, Arch. f. d. ges. Physiol., 1888, Bd. xliii., S. 69.

The epithelium of the alimentary canal represents a dialyzer membrane; on one side is the blood containing non-diffusible proteins, on the other the products of digestion containing diffusible proteins. If the salts in the contents of the alimentary canal make too strong a solution—*e. g.*, $MgSO_4$—water diffuses rapidly into the canal and a serous catharsis follows. In the usual relation between the blood plasma and the contents of the canal the water readily diffuses into the blood. Filtration was invoked to assist osmosis where that failed to satisfy the requirements. Brücke called attention to the fact that peristalsis causes an increased pressure in certain portions of the canal. The contraction of the villi empties them, driving the contents of the lymph radical on into the lacteals, and the contents of the capillaries on into the venules of the portal system. The valves in the lacteals and the veins prevent regurgitation of the lymph and blood when the muscles of the villi relax. The natural elasticity of the villi tends to cause them to regain their original size, thus making a negative pressure within the villi. Attention was also called to

FIG. 194



Relations of villi during peristalsis.

the fact that at the point where a peristaltic wave contracts the canal to one-half or one-third its usual lumen, the *apices* of the villi come together while there is still liquid around their bases (Fig. 194). A further contraction puts the liquid thus enclosed under pressure. The direction of this pressure will assist its filtration into the villi.

Absorption of fat globules was looked upon as a purely mechanical process in which the epithelial cells through their marginal rods or the lymph corpuscles engulfed the globules and transported them bodily to the lacteals. It was expected that this array of physical and mechanical forces would account for all the phenomena of absorption. More searching investigation on the part of the champions of the physical theory revealed the inadequacy of physical laws, as understood by physicists to account for the observed physiologic phenomena.

c. The Selection Theory.

The pendulum of thought has swung back toward the vital theory again. We do not use "vital energy" in our terminology, because the literature of the past prejudices us against that expression. We say knowingly that the cell "*selects*" the materials which are to be absorbed, but the mystery is as great in *selection* as when the thing was accomplished by virtue of a "vital energy." Moore sums up well our present views on absorption. "The cells of a secreting gland take up certain materials from the lymph in which they are bathed, and from these, in some manner, elaborate certain products which are passed into the gland lumen as a secretion. Similarly, the absorbing cells of the intestine take up certain products of digestion from the intestinal contents by which they are bathed, and build up from these certain materials which pass into the lymph (and plasma). *So that absorption may be regarded as a sort of reversed secretion. In both cases the process is a selective one.*"

The character and rate of the *secretion* are much influenced by the amount and the pressure of the blood in the gland; similarly the character and rate of absorption are influenced by the conditions which exist in the alimentary tract. Instead of looking upon the physical forces of diffusion and pressure as the *sole* factors of absorption we now recognize them as *modifying* factors.

The following are some of the facts which prove that the process of absorption is not one of simple diffusion: (*a*) Alkali albumin and acid albumin are practically indiffusible, yet they are readily absorbed from the large intestine, also from a loop of small intestine in the absence of all proteolytic enzymes. (*b*) "The rate of absorption, from the intestine, of various dissolved substances is not proportional to their diffusion coefficients." Röhmann[1] found that from a mixture of equal parts of Na_2SO_4 and dextrose the more slowly diffusible dextrose is much more rapidly absorbed than the sodium salt. *These facts and many others lead physiologists to attribute to the selective power of the living epithelial cells the typical phenomena of absorption, recognizing meantime that osmosis and filtration are modifying factors.*

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[1] Arch. f. d. ges. Physiologie, Bd. xli., S. 411.

THE PHYSIOLOGY OF ABSORPTION.

1. ABSORPTION FROM DIFFERENT PORTIONS OF THE ALIMENTARY CANAL.

a. Absorption from the Mouth.

That a certain amount of the soluble portions of the food is absorbed by the mucous membrane cannot be doubted. But oral absorption is solely incident to the sense of taste, and is too slight to be taken into account as a factor in nutrition.

b. Absorption from the Stomach.

The investigations of recent years tend to minimize the importance of the stomach, not only in digestion, but also in absorption. Before the subject was investigated with sufficient care it was taught that water and salts are absorbed freely by the stomach. It may be demonstrated, however, that only a very small proportion (about 1 per cent.) of the water is absorbed even when a considerable quantity of water alone is taken into the stomach.

Salts and sugars in solution are absorbed most readily when the degree of concentration is considerable; the minimum degree at which absorption may take place being 3 per cent. for salts and 5 per cent. for sugars; the most favorable degree of concentration being 20 per cent. for grape-sugar, while in the small intestine it is 0.5 per cent.

The proteoses and peptones are probably absorbed to a certain extent by the gastric mucous membrane; at any rate the presence of these products of gastric digestion greatly stimulates the activity of the gastric glands.

Alcohol is freely and rapidly absorbed by the stomach.

c. Absorption from the Small Intestine.

Absorption from the mouth and stomach seems to be purely incidental. If there is a specialized organ of absorption, that organ st be the villus of the small intestine. The villus seems to be cially fitted structurally for absorption; it is the organ which rbs nearly all of the liquid nutriment for the organism; no other tion may be ascribed to it.

hese considerations justify us in calling *the villus the organ of rption*.

rom the lumen of the small intestine the villi absorb the products gastric and of intestinal digestion; sugars, proteoses, peptones, y acids, soaps, water, salts, etc.

d. Absorption from the Large Intestine.

ater and salts are readily absorbed by the large intestine. This us seems to be an important site for the absorption of water, as intestinal contents pass the ileocæcal valve in a liquid state—ulating chyme—and enter the rectum in a pasty condition, the er having been largely absorbed.

bout 14 per cent. of the proteins and small amount of sugars and are also absorbed from the large intestine.

ost interesting of all is the fact that enemata of undigested ein, syntonin, or alkali albumin, even dilute egg albumen, is rbed in sufficient quantity to nourish an animal.

2. THE ABSORPTION OF DIFFERENT FOODSTUFFS.

a. The Absorption of Water.

s has been stated above, water is absorbed principally from the ll and large intestines. The portion absorbed from the former bsorbed mostly from the lower segment—viz., the ileum—while the first portion of the large intestine that takes up most of the er which remains in the intestinal contents when they pass the æcal valve.

he significance of these facts regarding the absorption of water ot difficult to see. If the water were largely absorbed in the ach and the upper part of the small intestine, the absorption of other products of digestion from the small intestine would be h hindered, because experiment has shown that the absorption he dissolved foodstuffs is much facilitated by dilute solutions. thermore, the movements of a viscous mass, deprived of most s water, would be much hindered.

ltogether it seems most natural and advantageous for the water e absorbed late in the general process of absorption.

b. The Absorption of Salts.

If the laws of diffusion dominate the process of absorption, and if osmotic pressure is the principal force involved in this process, we shall expect to see these physical laws and forces especially evident in the absorption of salts and their solvent water. The serous catharsis referred to above seems to be an example of a diffusion of water from the blood into the lumen of the intestine, induced by the high concentration of the salt solution in the intestine. When such conditions exist in a dialyzer, water passes through the membrane from the less concentrated into the more concentrated solution, while salt passes from the more concentrated into the less concentrated solution. The watery stools following ingestion of strong solutions of $MgSO_4$ and related salts seem to confirm this theory. Recent experiments by Wallace and Cushny[1] show that "Dilute solutions (isotonic) of the saline cathartics retard the absorption of fluid from the stomach and small intestine, and thus act by rendering (keeping) the contents more watery and more easily moved through the lower parts of the alimentary canal. . . . They (dilute solutions of the cathartics) do not necessarily increase the fluid of the bowel, but merely fail to be absorbed, and thus render the feces more fluid and more easily moved through the large intestine."

The same observers found that if a hyperisotonic solution of $MgSO_4$ be introduced into the intestine it is reduced to the isotonic condition by interchange with the blood; while if a hypoisotonic solution of $MgSO_4$ be introduced into the intestine it is raised to the isotonic condition by interchange with the blood, probably by giving up water to the blood.

If instead of using one of the salts, which clinical observations have led us to classify as cathartic salts, NaCl be used, it will be found[2] that dilute solutions (0.3 to 0.5 per cent.) are completely absorbed, both the water and the salt passing into the blood. Wallace and Cushny observed a similar phenomenon.

Evidently, then, the absorption of salts (and water) obeys the laws of diffusion more or less faithfully *according to the salt in solution.*

Why NaCl should pass the epithelial boundary so readily while the passage of $MgSO_4$ is practically barred out, can only be accounted for on the basis of a selective act on the part of the epithelial cells. From the accounts of experiments with the two classes of salts represented by NaCl and $MgSO_4$, one can scarcely avoid the conviction that the presence of such salts as $MgSO_4$ in the intestine affects the epithelium *by suspending its selective power and reducing it to a mere passive membrane subject to the laws of simple diffusion.* That such an effect, especially when produced by strongly hyperisotonic solutions, may be deleterious to the system is not unlikely. The question deserves investigation.

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[1] Intestinal Absorption and Saline Cathartics, American Journal of Physiology, July, 1898, vol. i., No. 4.

[2] Heidenhain, Pflüger's Archiv, 1894, vol. lvi., S. 579.

Summarizing, one may say: *The soluble salts, common in the foods, are readily absorbed by the epithelium of the small intestine. The absorption, though influenced by the laws of diffusion, responds primarily to the selective power of the epithelial cells.*

c. The Absorption of Carbohydrates.

The whole process of carbohydrate digestion points toward the monosaccharides as the form in which carbohydrates are to be absorbed.

The fact that only the monosaccharides, especially dextrose, may be found in the blood of the portal vein seems to confirm this indication. Rohmann[1] found that starch solution disappears rapidly from an intestinal loop. The succus entericus has almost no action upon starch. It must then be absorbed as starch by the epithelial cells. It leaves those cells as dextrose. The cells must, then, have the power to digest starch. Experiments of other investigators also point to similar conclusions.

Under the usual conditions, however, it is certain that by far the greater part of the carbohydrates is absorbed in the form of monosaccharides—*dextrose, levulose, galactose*—from the small intestine, and an unimportant fraction may be absorbed in the form of disaccharides, or even polysaccharides; a small proportion is absorbed by the stomach and large intestine.

d. The Absorption of Proteins.

As in the case of carbohydrates, so in the case of proteins, the processes of digestion are processes of solution and change from indiffusible to diffusible forms. That the solution of proteins is necessary would seem certain; yet, diluted, not dissolved, egg albumen is absorbed from the large intestine when given as an enema, and diluted egg albumen is absorbed (16 to 33 per cent.) from a loop of intestine in the absence of all proteolytic enzymes. Actual chemical solution is, then, not a necessary preliminary to absorption; it is only necessary that the protein be in a dilute liquid form. When the ideas of physiologists on this problem were made to harmonize with the osmosis theory, the reduction to a *diffusible* peptone was looked upon as a necessary preliminary to absorption. Though peptone is diffusible, its diffusibility is much too low and its rate much too slow to account for what actually takes place in the alimentary canal. Acid albumin or alkali albumin is absorbed from a loop of intestine almost as completely as are peptones and proteoses, though much more slowly than they (*i. e.*, about 60 to 70 per cent. in twenty-four hours—Huber, 1891). The amount of *leucin*, *tyrosin*, and allied bodies formed in normal digestion is probably very small because of the rapid absorption of the proteoses and peptones; naturally, then, the amount of these amido-acids normally absorbed will be small. A small amount of proteins is absorbed from the stomach, about 14 per cent. from the large intestine, and all the remainder—80 to 85 per cent.—from the small intestine.

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[1] Pflüger's Archiv, 1887, Bd. xli., S 411.

Summary: Of the proteins *a large proportion is absorbed by the small intestine in the form of proteoses and peptones. A small part of the proteins may be absorbed from the alimentary canal in the form of alkali albumin or acid albumin or even as native proteid.*

e. The Absorption of Fats.

The digestive processes of the small intestine change fat to a mixture of fatty acids, glycerin, soaps, and emulsified fats. The fatty acids are soluble in the bile acids. Glycerin and the sodium and the potassium soaps are soluble in water; calcium and magnesium soaps are soluble in the bile salts—probably changed to sodium soaps. The large amount of emulsion as compared to the amounts of the other forms found in the intestine, together with the discovery of innumerable oil globules in the epithelial cells during absorption, and the appearance of oil globules—emulsion—in the chyle of the lacteals during absorption, led physiologists to conclude that the fat is absorbed, for the most part, in the form of an emulsion. Earnest efforts have been made to reconcile this theory with the recognized limitations of fixed epithelial cells.

Before we accept the emulsion theory of absorption the following facts should be considered:

1. Ingested soluble soaps are absorbed.[1]
2. Soap and glycerin are absorbed and synthesized, after absorption and before the lacteals are reached, into neutral fat which circulates through the lacteals as a typical chyle emulsion. *The epithelial cells when treated with osmic acid show abundant oil globules.*[2]
3. Ingestion of free fatty acid and glycerin is followed by a synthesis within the epithelium and the appearance of fat globules there.[3]
4. Ingestion of free fatty acid *alone* was followed by the appearance of fat globules in the epithelial cells. In this case the cells must have furnished, from some source, the glycerin constituents of the fat formed.
5. Steapsin acts rapidly upon the fat and in the usual time con-

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[1] Radziejewski, Virchow's Archiv, Bd. lvi., S. 211.
[2] Perewoznikoff, Schafer's Physiology, vol. i. p. 451.
[3] Will, Arch. f. d. ges. Physiol., Bd. xx., S. 255.

in intestinal digestion would be able to change the usual it of fatty food into fatty acid and glycerin.[1]

t has been objected to the soap theory that the amount of)$_2$ necessary to saponify the fat of one meal would be three or mes as much as the whole body contains. Moore calls attention fact that once the soap passes into the epithelium the Na is of ther use in the cell and can be used over and over again as a . One can conceive of a sodium atom (I) being carried into testine as a part of the secretion combined with CO_2; (II) ing the CO_2 to join with a molecule of palmitic or other fatty nd passing into the cell; (III) dropping the palmitic acid for ; (IV) passing to the intestinal surface of the cell; (V) saponifying r molecule of palmitic acid carrying it into the cell; and again g with —OH, etc., repeating the cycle indefinitely. The form- of soap on the outer side of the epithelium is a spontaneous al reaction. The breaking up of that molecule to liberate ic acid for synthesis with glycerin and Na for synthesis with is probably due to a ferment action of the cell. Note that a vital force is called in at the critical point. The same force e invoked to put the NaOH out on the proper side of the cell.

atty acids are soluble in bile acids. A series of observations mann[2] and by his pupil, Krehl, show that the fatty acids dis- in the bile acids are absorbed, and synthesized into neutral ith formation of fat globules in the epithelium.

m the observations above cited it is evident: (I) that the rance of fat globules in the epithelial cells and the lacteals not necessarily demonstrate that the fat is absorbed as an on; (II) that the appearance of fat globules in the epithelial nd the lacteals after ingestion of soaps or of fatty acid and in does demonstrate that the elements of fats may be absorbed form and neutral fat synthesized by the cells from the elements; hat special cell activity is necessary in either case.

en two alternatives are presented the physiologist is wise to with suspended final judgment the one which is most reason- nd most in harmony with other similar processes.

mary: THE EMULSION THEORY *of fat absorption is that by greater part of the fat passes into the cells in the form of small es, neutral fat in emulsion, or of fatty acid in emulsion, while ute portion may be absorbed as soap.*

E SOLUTION THEORY *of fat absorption is that at the moment of g the epithelial cell the fat or fat elements are in solution either as in aqueous solution or as fatty acids in solution in biliary acids; e absorbed elements are synthesized in the epithelial cell, forming l fat which appears in globules, and that these globules pass he cells into the lacteals, forming the milky chyle.*

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[1] Rachford, Journal of Physiology, vol. xii. p. 92.

[2] Arch. f. Anat. u. Phys., Leipzig, 1889, Suppl. Bd., S. 86; cited by Moore.

CHAPTER VII.

METABOLISM: INTRODUCTION.

1. METABOLISM DEFINED AND CLASSIFIED.
2. METABOLIC TISSUES AND ORGANS: THE LIVER.
3. INCOME AND OUTGO OF MATTER.
4. WEIGHT EQUILIBRIUM.
5. THE CIRCULATION OF THE ELEMENTS.
6. THE CIRCULATION OF TYPICAL COMPOUNDS.
7. THE CHARACTER OF THE METABOLIC CHANGES.

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    - *b*. Circulation Form.
    - *c*. Metabolism.
    - *d*. Relation of Non-nitrogenous Metabolism to Muscular Work
    - *e*. The More Permanent Deposit of Carbohydrates.
    - *f*. Excretion of Carbohydrate Katabolites.
2. PROTEINS.
    - *a*. Absorption Form.
    - *b*. Circulation Form.
    - *c*. Metabolism.
    - *d*. Nutritive Value of Proteins.
    - *e*. Laws of Nitrogen Equilibrium.
3. FATS.
    - *a*. Absorption Form.
    - *b*. Circulation Form.
    - *c*. Metabolism.
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EMPERATURE TOPOGRAPHY.
EAT REGULATION OR THERMOTAXIS.

PATHOLOGIC PHYSIOLOGY OF METABOLISM.

ATHOLOGIC PHYSIOLOGY OF CARBOHYDRATE METABOLISM.

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IABETIC COMA.

B. DISTURBANCES OF FAT METABOLISM.

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PATHOLOGIC PHYSIOLOGY OF NITROGENOUS METABOLISM.

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PANCREATIC INSUFFICIENCY.
CTERUS.
HOLELITHIASIS.
OUT.

METABOLISM.

INTRODUCTION.

1. METABOLISM DEFINED AND CLASSIFIED.

The German physiologists were first to separate out from the eral territory of nutrition a special field in which to include those chemical processes by which matter is transformed from non-living nutrients to living protoplasm, and from living protoplasm to dead excreta. This *change* of *matter* was called *Stoffwechsel*; our technical term METABOLISM is used to cover the same field. Reference was made to the building up of nutrients into living protoplasm and to a reversed process. These chemical phases of metabolism are called, respectively, *Anabolism* and *Katabolism*. These terms are not so circumscribed, however, as might seem from the foregoing. *Anabolism* includes all those chemical changes by which molecular structure becomes more complex and *energy is made latent*; while *katabolism* includes all the chemical changes by which molecular structure becomes more simple and *energy is liberated.*

Besides the above classification, based on the character of the chemical change, we may classify the metabolic processes on the basis of the structures producing the change: (I) *Digestive metabolism* in the gastrointestinal tract; (II) *Special metabolism* in the organs particularly detailed; thyroid, thymus, suprarenals, and genital glands; (III) *Cellular general metabolism* in each cell, from material brought to it which is, however, also modified for use *in loco.*

2. METABOLIC TISSUES AND ORGANS: THE LIVER.

All specialized functions of the living organism are performed by specialized tissues or organs or systems of organs. Metabolism, however, is not a specialized function; it includes the chemical phases of every tissue activity, and is usually incidental to a primary function. For example: the primary function of the glandular tissues is secretion; but incidental to the secretion is a series of chemical changes which may be considered under the head of metabolism. In a similar manner muscular and nervous tissue possess primary functions peculiar to them and undergo metabolic changes in the performance of those functions. All active tissues, then, are metabolic tissues. The metabolic tissues may be classified as *muscular, nervous,* and *glandular.*

If there is an organ that may properly be classified as an organ of metabolism, that organ is the liver.

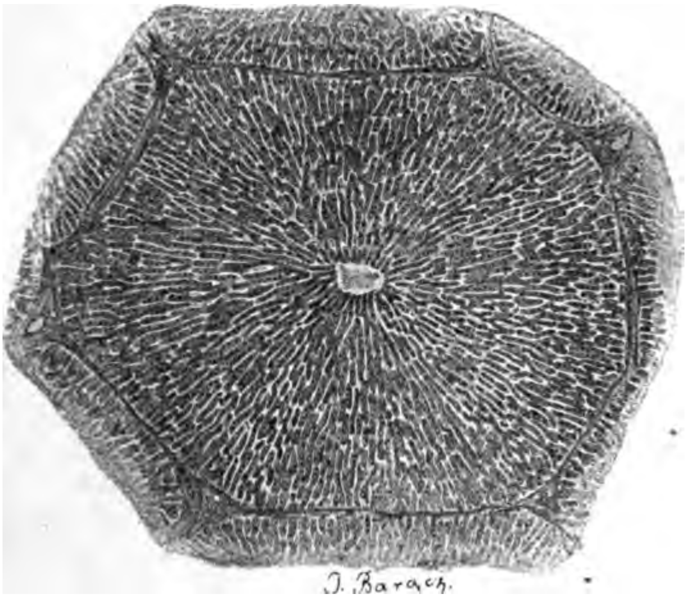
The *external secretion* of the liver is made up partly of substances which exert a more or less potent effect upon the processes of intestinal digestion, and partly of substances which are apparently simple excretions (bilirubin, biliverdin).

The *internal secretion* is composed either (I) of substances on their way to excretion, or (II) of substances which are to be subjected to further katabolism in other active tissues. To be concrete, the bile pigments, salts, and acids; the urea and uric acid, and the glycogen and dextrose are products of liver metabolism. Metabolism is the principal function. The liver is the great central whirlpool of the circulating nutrients; it is the centre of body metabolism; it may be called *the organ of metabolism.*

The anatomic features of the liver which are of special importance to the physiologist may be thus summarized:

1. The liver is supplied with blood from two sources: (*a*) *Portal venous system* from the capillaries of the intestines to the interlobular branches of the portal veins. (*b*) *Hepatic artery* bringing arterial blood which mixes with the portal blood within the lobule. Interposed then between an enormous absorbing, anabolic surface—the gastro-intestinal tract—and the rest of the body, the liver represents the extremely complex final katabolic surface.

FIG. 195



Diagrammatic representation of an hepatic lobule. (Szymonowicz.)

2. The hepatic veins collect the blood and carry it to the vena cava.
3. The biliary secretion is collected by minute bile capillaries—intracellular and intercellular—arranged in a fine meshwork, while on one side at least the liver cell is in close apposition with a nutrient bloodvessel from which it selects and elaborates the various ingredients of bile.
4. The biliary secretion is collected at the periphery of the lobule by the interlobular bile-ducts, and is poured into the duodenum during the digestive activity of that viscus.

a. The General Physiology of the Liver.

The phylogenic and ontogenic evolution of the liver consists of such physiologic and anatomic modifications that, from a gland primarily digestive or intestinal, it becomes one simultaneously *biliary*, *uropoietic*, and *hæmatopoietic*, and finally, in man and higher animals—subsequent to the growing function of the pancreas—it develops into an organ elaborating *most important internal secretions.* This role of the liver being thus foreshadowed by evolutionary changes comes to full expression in fetal life. In the human fœtus of one month it constitutes one-half of the total body weight; in the third month it amounts to one-third of the total weight; at term it weighs one-twentieth of the entire body and in the adult it equals one thirty-third of the body. In the ontogenic development the external, hæmatopoietic and biliary function gradually recede to give room for the internal secretions which, in the case of the liver, play perhaps a more important role than of any other organ.

FIG. 196

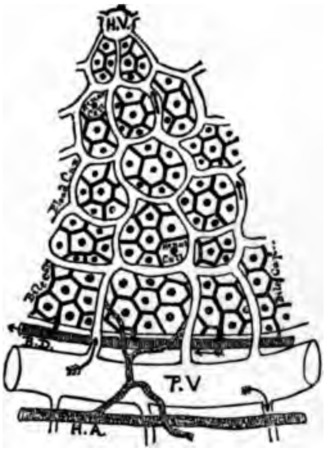


Diagram of the structure of the liver: *P. V.*, the portal or interlobular vein, which breaks up into the capillary network of the lobule; *H. V.*, central intralobular vein, a branch of the hepatic; *H. A.*, hepatic artery, supplying nutrition to the interlobular structures and terminating in the lobular capillary network; *B. D.*, the interlobular bile-duct which takes up the bile-capillaries at the periphery of the lobule. (Piersol.)

One of the most striking characters of the liver is the fact that it has *some functions highly specialized*, such as uropoiesis, elaboration of purin bodies

FIG. 197

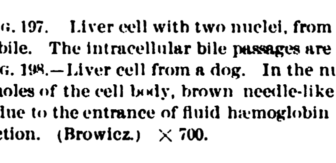


FIG. 198

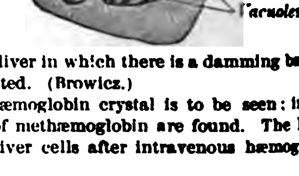


FIG. 197. Liver cell with two nuclei, from a human liver in which there is a damming back of the bile. The intracellular bile passages are much dilated. (Browicz.)

FIG. 198.—Liver cell from a dog. In the nucleus a hæmoglobin crystal is to be seen; in the vacuoles of the cell body, brown needle-like crystals of methæmoglobin are found. The latter are due to the entrance of fluid hæmoglobin into the liver cells after intravenous hæmoglobin injection. (Browicz.) × 700.

Good Plate Landois 303-4

PLATE III.

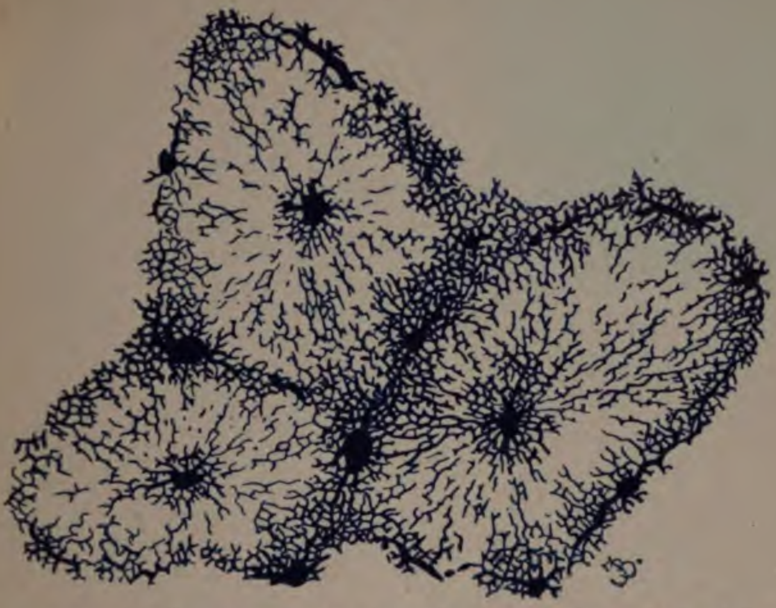


Fig. 1.—Bloodvessels of Three Liver Lobules of a Rabbit. In the centre of ch lobule is a central vein; at the periphery, the interlobular veins. × 60. zymonowicz.)

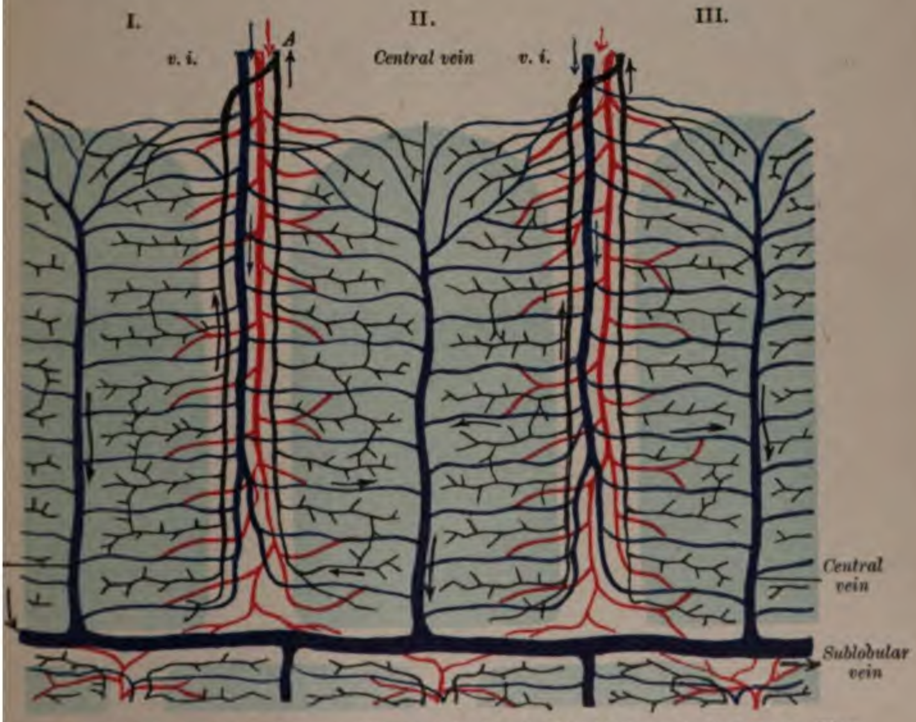


Fig. 2.—Diagram of the Liver. Three lobules (I., II., III.) are to be seen The ile passages are black, the arteries red, and the veins blue. *v. i.*, vena nterlobularis; *A*, duct. The direction of the circulation is indicated. Szymonowicz.)

ric acid, xanthin, hypoxanthin, guanin, etc.), chromopoiesis and e secretion of bile acids; while less specialized functions it shares th the pancreas (glycolysis) and with the hæmatopoietic organs ntizymotic and antitoxic action). Of all these hepatic functions re are two about which we know a great deal more than about ers: (I) its glycogenic activity and (II) the biliary function. This probably because the disturbances of these functions are more ickly and clearly manifested than is the case with other liver functions.

b. The Functions of the Liver.

1. ASSIMILATION OR METABOLISM.
    - (*a*) *Carbohydrate metabolism.*
        - (α) Glycogenesis.
        - (β) Glycolysis.
    - (*b*) *Fat metabolism.*
        - (α) Production or synthesis of fats, from proteins.
        - (β) Fixation of fat, lipopexy.
    - (*c*) *Proteid metabolism.*
        - (α) Proteolysis.
        - (β) Manufacture of NH_4 group, of uric acid, urea.
        - (γ) Elimination of tyrosin and of leucin.
2. BILIARY FUNCTION.
    - (*a*) *Secretory:* elaboration of bile acids.
    - (*b*) *Excretory:* or chromopoietic, elimination of pigments brought thither mainly by the phagocytic leukocytes.
    - (*c*) *Digestive:* in the intestinal canal, especially in the duodenum.
        - (α) Influence on action of pancreatic enzymes.
        - (β) Influence on peristalsis.
        - (γ) Inhibition of intestinal putrefaction.
        - (δ) Saponification of fats.
3. HÆMATOPOIESIS.
    - (*a*) *Hæmogenesis* (I) It regulates the hæmoglobin percentage of the blood by storing iron. (Kunkel.) (II) Actual hæmogenesis, very manifest in fetal life, and in the adult of subordinate role except in inflammatory conditions. The more remote from fetal life, the more will the liver give up its erythrogenic functions to the spleen and bone-marrow.
    - (*b*) *Hæmolysis:* a well-established activity, but whose role is not as yet well known.
    - (*c*) *Upon blood coagulation:* acting upon fibrin, elaborating coagulating and anticoagulating ferments.
4. UROGENESIS. Several constituents of the urine are formed in the liver to be transported by the circulation to the kidneys, where they are excreted.

(α) *Urea* is formed from such substances as ammonium carbonate, ammonium lactate, kreatin, glycin, etc.
(β) *Uric acid* is formed from midproducts of nucleoalbumin katabolism, probably from the *purin bodies*.
(γ) *Urates*, formed by conjugation of uric acid with metals.
(δ) *Various other* urinary constituents.

5. ANTITOXIC AND ANTIZYMOTIC FUNCTION.
  (*a*) *Toward microbic poisons.*
  (*b*) *Toward other exogenic poisons.*
    (α) Animal alkaloids.
    (β) Vegetable alkaloid: nicotine.
    (γ) Mineral poisons: heavy metals.

It has been conclusively shown that the liver transforms vegetable and animal alkaloids and diminishes their activity from 30 to 50 per cent. Furthermore, this antitoxic property is in direct proportion to its glycogen content. This has been proven for nicotine, phosphoric acid, etc.

  (*c*) *Detoxication of poisonous substances*, elaborated in the human body, by bacterial action in the intestines or otherwise. This is effected in various ways:
    (α) Sulphoconjugation of higher phenols—*e.g.*, indol to indican.
    (β) Production of ammonia radical, to counteract the fatty acids—*e.g.*, oxybutyric and diacetic acids.

6. ZYMOGENESIS. The liver forms several enzymes subject to classification as (I) *Oxydases* and (II) *Reducases*. The action of these enzymes is without doubt of great importance, but their relation to metabolism is at present somewhat problematic.

It is likely that the oxydases form a part of the defence of the organism by destroying toxins absorbed from the alimentary canal. The reducases may be the agent through which the organism builds fat from carbohydrates—a process which requires a reducing agent.

3. THE INCOME AND OUTGO OF MATTER.

The manifestations of life are the manifestations of kinetic energy. In the animal organism the energy is received as potential chemical energy and expended almost wholly as kinetic energy. As far as it is known, energy exists in nature only in association with matter: gravitation, motor motion, chemism, heat, and light are all intimately associated with matter, and if transmitted, that transmission can take place only through the agency of matter. If, then, the animal organism is to receive, transform, and expend energy it must receive, transform, and excrete matter. The whole process is called nutrition. We have followed the process through the reception of food materials into the alimentary canal, their partial transformation (their digestion) in the stomach and intestine, and their absorption into the organism. The amount of the income is the amount of absorbed matter, and the amount of the outgo is the sum of the excretions from kidneys, skin, lungs, etc.

4. WEIGHT EQUILIBRIUM.

If the absorbed matter equals in weight the excreted matter, the ody will neither increase nor decrease in weight; it will be in *equi-brium.* Perfect equilibrium seldom exists; during youth there is a radual increase in weight; during adult life there is approximate uilibrium, while during the senile period there is usually a gradual crease in the body weight. But this only indicates the general urse of the curve of income and outgo. Many factors enter into e problem of body growth and equilibrium to cause numerous inor curves to be superimposed upon the general curve. The currence of one or two large waves on that part of the curve which presents the period of growth gives rise to the "*wave theory of owth.*" Besides these large waves there are small waves occurring ach year, and possibly even smaller diurnal waves.

The *physiologic test* of equilibrium is made by taking the weight t short intervals. The method is like getting an idea of business by oting the daily balances; it shows the equilibrium, but gives only a vague idea of the magnitude of the exchange between debits and credits. In the *chemical* test of equilibrium, on the other hand, the debits and credits of an organism are determined by finding the quantity of absorbed material and by determining the quantity of urea, water, and carbon dioxide excreted. If the nitrogen of the gesta equals the nitrogen of the ingesta, the organism is said to be n a state of "nitrogen equilibrium." If the total egesta equals the otal ingesta the organism as a whole is in a state of equilibrium.

5. THE CIRCULATION OF THE ELEMENTS.

This is one of the most interesting and important chapters of physi-ology; it is the most striking proof of the conservation of energy. Every constituent of the human body circulates in some form or ther, be it solid, liquid, or gaseous. It moves and is moved to and rom the place of activity assigned to it by unknown, but yet xisting, forces. Like every cell, these circulating elements have their ycle of activity; electively absorbed and assimilated; kept somewhere n the body inaccessible to harmful conditions, ready for use, trans-erred thither, used in the great laboratory of the body, and then emoved by special conveying agents to organs particularly entrusted with their final removal from the system. The mechanism of this circulation in the human body is very little known as yet, but even those few established facts are well calculated to excite the continual admiration of the thinking physiologist.

The minerals incorporated into the system undoubtedly perform greater service to the economy than we usually ascribe to them. Their influence upon ferments—oxydases and reducases—is now generally admitted. Iron, iodine, manganese are the vital agents in some of the essential functions of human existence. The chlorides play an extremely important role in the protective detoxicating agencies of the body. Again, phosphorus is a necessary ingredient of animal tissues.

(*a*) **Carbon.**—This element enters the system as an important constituent of all the foodstuffs. It is built up into all of the tissues and eventually it is combined with oxygen to form CO_2, which is excreted by the lungs in the gaseous form, or it may be combined with O, N, and H in urea or uric acid, etc., and excreted by the kidneys.

(*b*) **Hydrogen** enters the system as a constituent of all foodstuffs, including water. Like carbon, it is a constituent of all tissues. It is excreted in the form of H_2O by kidneys, skin, and lungs; though a part is excreted as a constituent of urea, uric acid, and allied bodies. Most of that hydrogen which enters the system combined with oxygen in water leaves the body as water, never having been separated from the oxygen.

(*c*) **Nitrogen** is brought to the system only through the protein foods. It is a necessary constituent of all active tissues, muscle tissue, glandular tissue, and nerve tissue. In the metabolism of the tissues it is, step by step, freed from its complex combinations until finally it is excreted by the kidneys with C, H, and O in urea, uric acid, etc.

(*d*) **Oxygen** enters the system uncombined and variously combined. As a gas it enters the lungs, is taken up by the hæmoglobin, transported to the tissues, where it plays a prominent part in katabolism. It finally leaves the cell combined with H in H_2O, with C in CO_2, or with C, H, and N in urea or uric acid. In these forms it is excreted by the lungs, skin, or kidneys. A large quantity of oxygen enters the system in combination in the various foodstuffs. This part of the oxygen is excreted in the same combinations as the oxygen of respiration.

(*e*) **Phosphorus** enters the system with the proteins. Though phosphorus is a constituent of few protein foods (nuclein, nerve tissue, blood plasma, lymph, and milk), one or more of these is usually associated with each kind of nitrogenous food, so that the system receives a considerable amount. In the body it is a constituent of the tissues and fluids enumerated above; and, combined as $Ca_3(PO_4)_2$, it is a most important constituent of bone. It is excreted by the kidneys as calcium, magnesium, or ammonio-magnesium phosphate.

(*f*) **Sulphur** is received in combination in proteins, is built up into the body proteins, and is excreted by the kidneys as free sulphuric acid, or as $HKSO_4$ or $HNaSO_4$, or it may be joined to phenol as phenolsulphuric acid, phenolsulphate of potassium, etc.

This element plays a prominent, although defectively known, role in the economy. We ingest with our daily quantum of proteins (107 grams, Gautier) 1 gm. of sulphur; four-fifths of this is metabolized and give rise to 2 gm. of anhydrous SO_3 per twenty-four hours. As measured by the daily output of sulphur in the urine, etc., there are two ways in which sulphur is used in the system:

(*α*) ACID SULPHUR COMPOUNDS: sulphur esters of katabolized proteins.

(I) Employed to detoxicate by sulphoconjugation of phenols and other products of albuminoid disintegration. They form 8 to 12 per cent. of the total sulphur of the urine.

(II) Used in the osmotic interchange of nutritive substances between the cells and their surrounding medium by combining with such bases as Na, K, Ca, Mg (of these latter sulphates about 4 gm. per day are excreted).

(*β*) NEUTRAL SULPHUR COMPOUNDS, that is, such as are derived directly from the katabolized cell and *nuclein* protoplasm. Into this group come the alloxur bodies, uric acid, alloxyproteinic acid, uroferric acid, etc. Neutral sulphur metabolism has a normal constant equilibrium varying only in different individuals, while the oxidized or sulphur esters vary with different individuals and in the same individual.

(*g*) **Chlorine** enters the body in combination with sodium. As far as is known, it is separated from this combination, if at all, only in the parietal cells of the peptic glands. That part of the HCl which is absorbed from the alimentary canal comes into contact with Na_2CO_3 or $NaHCO_3$ of the blood and forms H_2O, CO_2, and NaCl, which are excreted.

(*h*) **Iron** is the most important of the metals and at the same time it is the most difficult one of them to absorb and assimilate. Recent investigations of Bunge and others demonstrate that iron may be assimilated and built up into hæmoglobin only when it is absorbed in the form of an organic compound. Whether it is necessary that it should be received into the alimentary tract in the organic form, or whether it may be raised, by the process of digestion, from the inorganic to the organic combination and be absorbed and assimilated, was for a long time a debated question; but investigation has demonstrated that even in the form of a chloride the iron is raised to a peptonate or albuminate in the alimentary tract and absorbed.

Iron is an essential of hæmoglobin, and is also found in every cell of the organism, but in the living protoplasm no known chemical test can reveal its presence because the metal is so masked or covered up by another substance or substances that no deleterious agent can attack it during the normal life of the cell. According to Gautier, the system needs 60 to 90 mgm. of iron per day. It is absorbed in the duodenum at the rate of about 1 centigram per day, is stored as organic iron in the liver, and is then excreted in the large intestine, 60 mgm. of iron per day in the feces of a normal adult on mixed diet. (Gautier.)

In anæmia from severe hemorrhage the hæmoglobin is quickly replenished from the iron in the liver, not from the iron ingested there; so that in a healthy individual the blood is quickly replenished, and in a weakened one recovery is necessarily slow.

There is a normal iron equilibrium in the body which is regulated in various ways. It is stored in the liver, especially in the fœtus and the newborn, and bone-marrow of the adult (and also in the uterine mucosa and mammary gland of adolescent animals and women). These depots, of which the liver is the most important one, distributes the metal to the system as the need requires. We witness, then, a normal transfer or circulation of iron. A fresh supply of it absorbed, stored in the liver, etc., in a form as yet unknown, is then given off to the cells of the blood and of the hæmogenetic tissues—*e. g.*, the spleen, bone-marrow, the lymphatic glands—to form hæmoglobin, which, when it has served its purpose, is again carried to the liver and spleen by the scavenger leukocytes and transferred into pigments for different purposes, mainly excretory. During prenatal period of human life iron plays a very important role. The red blood corpuscles are nucleated and contain a very much higher percentage of iron than in the adult. Moreover, the liver in the newborn contains five to ten times more iron than the adult organ. This surplus of iron helps to tide the newborn over the first days of change from nutrition *via* the maternal blood to a self-supporting existence.

The exact vital role of iron in the economy is said to be similar to that of Mn in the ferment lactase, or Ca in the coagulating ferment thrombase.

After iron has served its purpose it may be excreted by the kidneys, by the epithelium of the intestines; even a small part is lost with the cuticle, hair, nails, etc.

(*i*) **Arsenic** is a widely distributed constituent of every soil, nearly every metallic ore and mineral waters, even, according to Gautier, in minimal quantity constantly present in our kitchen salt, and we no longer wonder that it is actually an ingredient of every tissue of the human organism. The thyroid gland and the thymus body contain the largest share of this metal, while 15 gm. of hair contain $\frac{5}{1000}$ to $\frac{6}{100}$ of 1 mgm. of arsenic, as shown by the Marsh test. This ubiquity of arsenic being established, we can easily understand why the post-mortem finding of arsenic in human tissues should never mislead experts in their medicolegal testimony.

When arsenic is ingested it is absorbed and enters the liver, where it combines to form stable compounds. The role of arsenic in the economy is similar to that of phosphorus, and it is perhaps an ingredient of unstable bodies comparable to ferments.

(*j*) **Other Metals** are usually assimilated in chemical association with organic foodstuffs, and are excreted by the kidneys. A small amount of sodium, calcium, etc., is secreted by the pancreas and the liver, and is poured into the alimentary canal. A part of these metals is reabsorbed in combination as soap; all that is not reabsorbed is lost, in this way, to the organism.

6. THE CIRCULATION OF TYPICAL COMPOUNDS.

(*a*) **Water.**—Our remote ancestry had undoubtedly an aquatic habitat. It has been said that "man is, in a sense, an aquatic animal." It is true that about 60 per cent. of the body is water, that every active cell of the body is bathed in liquid, and that even the surface of the body is, during health, usually covered with a film of moisture in the form of "sensible" or "insensible" perspiration. The organism can live many days without solid food, but deprivation of water for a very few days suffices to cause death.

The water is in part taken with the food and in part taken as drink. Water which is taken as such undergoes no change while in the system, except that an occasional molecule is joined by *Hydration* to some organic molecule. It is absorbed by the intestinal epithelium, even when it is taken between meals; when it is taken with a meal it is likewise passed on into the intestine with the chyme, to be absorbed by the intestinal epithelium. Water is the general solvent and diluent of the system. It makes possible the absorption of the digested foods and the excretion of waste products. Of all the water excreted by the kidneys, skin and lungs, a large part is water which enters the system as such; another part is the product of the oxidation of the hydrogen of the tissues in katabolism, while another portion has been released from complex molecules by dehydration.

(*b*) **Sodium Chloride** is taken as such with food. It is in solution in all the fluids of the body. It probably assists in endosmosis. It is probably the source of the chlorine element of the HCl of the gastric juice. (See "Secretion of HCl.") Sodium chloride may be formed in the system. It may be formed in the organism by a combination of absorbed hydrochloric acid with the carbonate of bicarbonate of sodium, as suggested under "*chlorine.*" It is excreted by the kidneys and skin and is secreted by lacrymal glands and salivary glands. It is in fact a constituent of every secretion and excretion.

(*c*) **Other Compounds** in this class are of not very great physiologic importance.

7. THE CHARACTER OF THE METABOLIC CHANGES.

a. Synthesis and Decomposition.

Synthesis is applied in chemistry to the construction of a molecule from simpler components; while decomposition is the reverse process. The combination of a fatty acid with glycerin is a synthesis, while the breaking up of a fat into the two constituents is an example of a decomposition.

b. Hydration and Dehydration.

These terms signify the addition or subtraction of molecules of water; it is only a specialized sort of synthesis or decomposition. Hydrolytic changes are especially common in the digestive process. Recall the addition of a molecule of water to the molecule of starch followed by a cleavage (hydrolytic cleavage) of the hydrated molecule into dextrine, and a second molecule of water to maltose to make dextrose, while the dehydration of the same molecule of dextrose takes place in the liver, after absorption, reducing the dextrose to the amylose radical ($C_6H_{10}O_5$), which taken *n* times is synthesized into a glycogen molecule $(C_6H_{10}O_5)_n$.

c. Reduction and Oxidation.

These terms need no explanation. In plants the reduction processes predominate and the liberated oxygen escapes into the general atmosphere. During reduction processes energy is used to consummate the change and energy is made latent. In the animal kingdom oxidation processes predominate; oxygen is taken from the atmosphere to consummate the change and carbon dioxide is returned to the atmosphere. Oxidation liberates latent energy.

SUMMARY: "*The chemical processes of the animal organism may be represented as a series of syntheses and decompositions, or of anabolic and katabolic changes, by virtue of which the highly complex and slightly oxidized constituents of the body and of foodstuffs are decomposed into simple and highly oxidized compounds, which are removed from the body by the various organs of excretion.*" *The difference between the potentiality of the ingesta and the egesta represents the potential energy liberated in the organism as the kinetic energy of life.*

ANIMAL METABOLISM.

A. THE METABOLIC CHANGES OF DIFFERENT CLASSES OF FOODSTUFFS.

a. Carbohydrates.

Every tissue and cell in the human body participates to a certain extent in the metabolism of carbohydrates. But phylogenetic and ontogenetic studies show us that in man and higher animals certain tissues are specially entrusted with (I) the utilization of sugars; (II) the supervision of carbohydrate metabolism and, in fact, the hypoblastic derivatives lead in this activity, while the muscles play only a secondary role. The control and direction, however, of the entire sugar metabolism in the body is exercised by the central nervous system. Certain portions of the hypoblastic layer have become specifically differentiated for this one function. Many and conclusive evidences support this statement.

Organs and tissues recognized as manifest participants in the metabolism of sugars: (I) The liver; (II) the pancreas; (III) the muscular system; (IV) other active tissues.

1. Absorption Form.—It will be remembered that during the process of digestion the carbohydrates are for the most part changed to dextrose. There is no evidence that other diffusible or even indiffusible carbohydrates may not be absorbed—*i. e.*, pass into the epithelium of the alimentary tract; all the carbohydrate matter found in circulation in the portal system is, however, a monosaccharide. It is evident then that if cane-sugar is absorbed by the epithelium, it undergoes hydrolytic cleavage in the epithelium; so that in whatever form the carbohydrate is absorbed it is changed to dextrose or to some other monosaccharide by the epithelium and passed into the capillaries of the *portal system.*

2. Circulation Form.—In the blood all sugars normally appear as monosaccharides, probably dextrose. The blood of the portal vein may have as much as 0.3 per cent., while that of the general circulation has usually about 0.1 per cent. Furthermore, the above-mentioned high percentage for the portal circulation may be observed only after a meal rich in carbohydrates, while the amount quoted for the general circulation is more or less constant. The blood which enters the liver may have 0.3 per cent. dextrose; the blood which leaves uniformly has 0.1 per cent. dextrose. With these facts in view, it is evident that the liver must effect a profound change in the carbohydrate material brought to it by the portal system.

3. Metabolism of Carbohydrates. (*a*) **As Influenced by the Liver.**—The relation of the liver to sugar metabolism is an extremely close one and exemplified by a number of well-established actions: (α) glycogenesis; (β) glycolysis; (γ) glycopexy or storing of glycogen. The blood entering the liver after a meal brings a much larger amount of carbohydrate material than is carried away by the hepatic vein. That this excess of carbohydrates must be stored in the liver is the necessary conclusion; yet if a freshly excised liver be tested for dextrose that substance will not be found in greater quantity than may be accounted for by the portal blood present. A special treatment reveals another form of carbohydrate—glycogen.

(α) GLYCOGENESIS.—Glycogen $(C_6H_{10}O_5)_n$ was discovered and described by Claude Bernard in 1857. Bernard's theory as to its relation to general nutrition is substantially the one which is accepted to-day. Briefly outlined the preparation of glycogen is as follows: (I) Kill an animal after a heavy carbohydrate meal. (II) Excise liver, hash same, and plunge it into boiling water, which has the double function of extracting glycogen and of stopping post-mortem change of glycogen to dextrose. (III) Filter. The opalescent filtrate contains glycogen or "animal starch." If one subject this animal starch to the iodine test a *wine color* will result. The microscope reveals the presence of glycogen in liver cells, deposited in the substance of the cytoplasm. But the carbohydrates do not represent the sole source of glycogen; for an animal deprived of both carbohydrates and fats will still form glycogen in the liver on a pure protein diet. Such is not the case, however, on a pure fat diet. Whether with a mixed diet of carbohydrates and proteins a part of the proteins are used in the formation of glycogen remains yet undetermined.

The formation of glycogen is common to all cells, especially when stimulated by such influences as the embryonal stage, inflammation of any kind, neoplastic influence, or generative processes (Brault-Loeper), but it is a particular function of the liver. Chemical and histochemical proofs of the presence of glycogen in all protoplasma are well established. Glycogenesis in the liver varies within narrow limits while its biliary function ranges between widely separated, yet withal normal limits, because the former is a secretory activity and the latter mainly an excretory one.

Glycogen forms in the fœtus 12 to 15 per cent. by weight of liver and 3 to 4 per cent. by weight of the normal adult liver, but during digestion it may reach 20 to 80 per cent. by weight. The daily output of glycogen is about 1800 gm.

(β) GLYCOLYSIS.—In plants the starch formed in the chlorophyll grains of the leaves must be changed to a soluble form—dextrose, for example—before it can be carried by the circulatory system of the plant (fibrovascular system) to distant parts of the organism for deposit, or for further metabolism. In animals the glycogen is only temporarily stored in the liver. It is to be used in the general metabolic tissues of the body—for the most part the muscles. It cannot be carried to the muscles in the insoluble form in which it is deposited in the liver. The liver possesses an amylolytic ferment which changes the animal starch to dextrose. In this soluble and diffusible form it enters the circulation, is carried to the metabolic tissues, absorbed or "selected" by the active cells of these tissues, and is by them metabolized. Just at this point we enter a controversial field. All are agreed that within the muscle cells the dextrose is subjected to a series of metabolic changes whose ultimate result is the liberation of energy. Some believe that before the foodstuff can yield to the animal organism its potential energy *it must be built up by the cell into living cell protoplasm.* Others believe that the energy of the foodstuffs may be *directly* liberated without the necessity of a long series of anabolic changes preceding those katabolic changes which must finally liberate the energy. Here are certain facts which deserve consideration in this connection:

(I) If dextrose is first built up into muscle protoplasm, all katabolism of the nitrogenous cell protoplasm should result in the liberation of nitrogenous compounds. The katabolism incident to muscle contraction should yield such nitrogenous katabolites in proportion to the muscular energy expended. But these nitrogenous katabolites are further changed and appear in the excreta as urea, CO_2, and H_2O. The urea then should be a measure of muscular work; but urea does not essentially vary with varying muscular activity. The hypothesis that the dextrose is anabolized to the plane of cell protoplasm is not in harmony with the facts of excretion and the evidence is strong against the hypothesis. (II) If dextrose may be directly katabolized, the katabolites (CO_2 and H_2O) should vary with muscular activity. But excretion of CO_2 and H_2O varies directly with muscular activity. This is in harmony with the facts of excretion and is strong evidence in its favor.

(*b*) **As Influenced by the Pancreas.**—The role of the pancreas in the utilization of sugar is a very important one. Its anatomic relations with the liver and duodenum on the one hand, and with the vascular system on the other, support this role. Besides its prominent part in general metabolism the pancreas secretes a ferment, which enters the blood by way of the lymphatics, and then in the tissues (not in the blood itself) acts as a glycolytic enzyme. Recent investigations have proven that the so-called glands of Langerhans are detailed to secrete this enzyme. They are (endocrinous) compact, vascular, interacinous collections of lymphoid-like cells, particularly numerous toward the splenic end of the organ. They were discovered by Langerhans (1869), best described by Renant (1879) and their pathogenic importance set forth by the famous experiments of Mering-Minkowski. Basing themselves upon the observations of Lancereaux and Laguesse, these two scientists established the nosologic value of these cell groups in glycosuria, and, furthermore, they give a powerful impetus to the clinical and experimental study of the pancreas. Without going into the details we will summarize here the conclusions from the respective works of the last twelve years:

(I) Diabetes is not a nosologic unit; it may be due to lesions outside of the pancreas, as shown by (piquere) puncture, disease of the fourth ventricle, phloridzin diabetes, acromegaly, etc.

This in spite of the fact that in some species of animals total extirpation of the pancreas produces genuine diabetes.

(II) We have enough anatomic and clinical facts to prove that diseases of the pancreas may be considered as an important cause of glycosuria. This holds true in man and in the other animals. There are some cases of true diabetes in which no macroscopic or microscopic lesions of the organ can be found, although in the great majority of cases the islands of Langerhans present scleroticoatrophic lesions. On the other hand, total destruction of the pancreas, in man, through disease, is sometimes unaccompanied by glycosuria, and it is just here where the harmony between clinical and anatomic evidences is lacking.

A priori one would conclude that to an organ which, like the pancreas, acts vicariously for the stomach (proteolysis), for the liver (amylopsis), and for the intestines (lipolysis), could not logically be attributed an autonomous action in sugar metabolism. To the thinking observer it must appear that: (I) The metabolic synergy of the organs and tissues—salivary glands, hypophysis cerebri, liver, pancreas, glands of Lieberkühn (Lepine)—is manifested in diseases as well as in health. These different tissues act in harmony with the nervous system to keep the remarkable sugar equilibrium of the blood (0.1 to 0.27). A vicarious action of the one will more or less fully compensate for the diminution in function of the other. (II) It would be poor husbandry if nature were to assign so vital a function as sugar metabolism to a single small organ.

(*c*) **As Influenced by the Nervous System.**—The guiding and directory action of the nervous system upon sugar utilization, foreseen by Boerhaave, was for the first time proven by the experiments of Claud-Bernard over fifty years ago. Other scientists of his school put the nervous factor upon a still more firm basis (Seegen, Frerichs, Kussmaul). As a result we know to-day that the role of the nervous system upon sugar metabolism is about this: There exists in the medulla oblongata a centre which, upon impulses received by way of the trophic nerves and other unknown roads, influences the various organs connected with the husbanding of carbohydrates in the system, and prompts them to the performance of their allotted function. Clinical observers have furnished us the greater number of facts regarding this influence. The role of the nervous system upon the onset, course, and nature of glycosuria is so generally appreciated that it is needless to enter into the details.

4. Relation of Non-nitrogenous Metabolism to Muscular Work.—The experiments of Voit and Pettenhoffer (see pp. 468 and 470) with men and animals in respiratory chambers demonstrate that the energy of muscular work, *under normal conditions, comes mainly, if not exclusively,* from the oxidation of non-nitrogenous material.

5. The More Permanent Deposit of Carbohydrates.—That this occurs not in the form of carbohydrates, but in the metabolized form of fat has been demonstrated. A part of the carbohydrate foodstuff in circulation as dextrose is absorbed by living connective-tissue cells and transformed into fat which is deposited in the cells and held as a reserve of potential energy, to be called out when more easily metabolized glycogen and dextrose are insufficient for the needs of the system. What is the character of the change the dextrose molecules must undergo to make palmitin? We know that palmitic acid is readily synthesized with glycerin to form tripalmitin. The storage of fat must involve the following general changes:

1. 3 × palmitic acid $= 3(CH_3(CH_2)_{14}COOH) = 3(C_{16}H_{32}O_2) = C_{48}H_{96}O_6$.
2. 8 × dextrose $= 8(C_6H_{12}O_6) = C_{48}H_{96}O_{48}$.
3. 8 dextrose + glycerol = tripalmitin $+ 3H_2O + 42O$.

The formation of fat from dextrose must be attended by the liberation of oxygen. This is an anabolic process to consummate which requires energy amounting to about 5500 calories per gram fat. That it takes place in one reaction as written above is not probable. That it is eventually a combination of dextrose and glycerol is an undemonstrated hypothesis. *That the process, whatever it may be, is an anabolic one attended with the liberation of oxygen and the making latent of energy is beyond question.*

6. Excretion of Carbohydrate Katabolites.—The katabolism of carbohydrates yields CO_2 and H_2O. These waste materials are excreted by the lungs, skin, and kidneys, unchanged or recombined, but for the most part unchanged.

b. Proteins.

1. Absorption Form.—Most proteins enter the epithelium from the alimentary canal as peptones and proteoses. A small portion may enter as acid albumin or alkali albumin or even as native protein. Within the epithelium these proteins undergo a change. Evidence of this is cited in the facts that neither peptone nor proteose is found in either blood or lymph; and that when either of these substances is injected into the circulatory system it is promptly excreted as such. The living cells of the intestinal epithelium must be able therefore to transform the proteins absorbed into the normal proteins of the circulation. This consists in a recombination of simple nitrogenous molecules into more complex ones with liberation of water.

2. **Circulation Form.**—The blood contains plasma proteins—serum albumin and serum globulin—and corpuscle proteins. There can be no doubt that the absorbed protein foodstuff enters the plasma, increasing its quantity of one or both proteins. There is no storehouse for reserve proteins except so far as the circulation itself serves such a purpose. The *absorbed protein,* transformed through the metabolic activity of the cells of the intestinal epithelium into serum albumin and serum globulin, *is received by the portal system* and thence distributed to the system as constituents of blood plasma, lymph plasma, and tissue plasma. Every living cell of the system may select from the plasma which bathes it such variety and quantity of the plasma proteins as are necessary in carrying on the cell activities.

3. **Metabolism of Proteins.**—As in the case of carbohydrates, so here, the question as to whether or not all katabolism of proteins proceeds from living cell protoplasm is a controversial one. Many of the cycologists would answer the question affirmatively. There are strong indications amounting almost to a demonstration, that only a part of the protein is anabolized to the plane of living cell protoplasm while a part is directly katabolized. Among the considerations favoring the second position one may mention: (I) The correspondence of protein katabolism rather to the variation of protein consumption than to special cell activity. This is especially marked in the case of the muscle metabolism and will be treated later. (II) Albuminoids—*e. g.*, gelatin—cannot be built up into tissue, though they may be used as energy-producing nitrogenous foods.

The preponderance of evidence in favor of the view that not all proteins are first raised to the plane of living protoplasm before being katabolized leads to the division of the protein supply into two parts: (I) *tissue-producing proteins,* and (II) *energy-producing proteins.* This division corresponds roughly to Voit's classification into "organ protein and circulating protein." It is now believed that *all metabolic changes are either intracellular or are produced by enzymes,* so that Voit's terms seem less appropriate than the terms suggested above. The tissue protein is that portion of the nitrogenous foodstuff which is built up by the cells into *living protoplasm.* The energy-producing protein is that portion which is directly katabolized *within the cell under the influence of the living protoplasm,* and serves the sole purpose of producing energy. It must not be forgotten that the tissue protein in its final katabolism incident to the special activity of the cell yields energy also. Whether one follows the change of tissue proteins or of energy-producing proteins he eventually considers the decomposition—direct or indirect—of a nitrogenous foodstuff from the protein level to the urea level. In general proteins represent about 5750 calories per gram of protein, while the unavailable energy of a gram of protein represents 1650 calories; the net energy represented by one gram of protein being about 4100 calories.

Hofmeister's formula for albumin will give us some idea of the complexity of a typical protein: $C_{204}H_{322}N_{52}O_{66}S_2$. The nucleoproteids differ in their general constitution by the presence of phosphorus, while the chromoproteids contain iron. Much remains yet to be determined regarding the specific changes which protein undergoes in its decomposition. This much is known: (I) Some of the protein is reduced to CO_2, H_2O, NH_3, SO_3, etc., and these in part recombine, forming urea in which NH_3 is combined with C, O, and H, or forming sulphates in which SO_3 is combined with metals or with indol, skatol, etc. (II) Some of the protein is changed more directly to urea and uric acid—glycocoll, leucin, kreatin, sarcolactic acid, ammonium lactate, succinic acid, amido-acids, arginin, cystin, and cystein being midproducts of the katabolism.

The observations of Gaglio, Frey, Marfori, Minkowski and others[1] make it certain: (I) that sarcolactic acid is formed in various metabolic tissues; (II) that it circulates in the form of the acid or ammonium lactate in the blood; and (III) that it is changed in the liver to uric acid and certain by-products.

There is no positive proof that kreatin is a forerunner of sarcolactic acid. The probabilities are favorable to such a relation. The course of katabolism may be assumed to be something as follows:

(1) Kreatin + 3O = CO_2 + urea + glycocoll.
(2) 2 Glycocoll = urea + sarcolactic acid (CH_3—CHOH—COOH).
(3) Sarcolactic acid + NH_3 = ammonium lactate.
(4) 2 Ammonium lactate + 12O + NH_3 = $2CO_2$ + $2H_2O$ + ammonium carbonate. [$O:C:(ONH_4)_2$].
(5) Ammonium carbonate—H_2O = ammonium carbamate.
(6) Ammonium carbamate—H_2O = urea.

Here is another possibility: Kreatin may be subjected to a hydrolytic cleavage into ammonium lactate and carbonate:

(1) Kreatin + $4H_2O$ = ammonium lactate + ammonium carbonate.
(2) Ammonium carbonate—$2H_2O$ = urea.
(3) Ammonium lactate + amido-acids = uric acid + CO_2 + H_2O.

Note (1) that the series of changes suggested here represents a step by step process by which a complex body is reduced to a series of simple bodies; (2) that the processes are, with one exception (3), oxidations, dehydrations and decompositions.

As is already indicated above, the kreatin of the body has two sources. A part comes from the ingested lean meat and is dehydrated in the liver, forming kreatinin; a part is formed in the muscles and is probably changed at once to urea, CO_2 and glycocoll, or to sarcolactic acid, urea, and CO_2.

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[1] Quoted by Schafer, Text-book of Physiology, vol. I. p. 905.

As with kreatin so with leucin, there are two sources in the system of an omnivorous or a carnivorous animal: (I) From the alimentary tract where leucin is a product of trypsin decomposition of peptone. A part of the leucin so formed is absorbed and carried to the liver in the portal circulation. (II) But aside from this source leucin is one of the midproducts of normal protein katabolism and is found in small amounts in all liquids of the body. In due time it makes its journey to the liver with the general circulation, and in that organ is further katabolized to its simpler elements, and is excreted as urea, CO_2, and H_2O.

That the liver is the seat of this change is practically demonstrated by the observation that when the liver becomes extensively diseased leucin accumulates in the blood to a more than normal degree and is finally excreted unchanged by the kidneys.

Glycocoll, or glycin, may be considered a normal midproduct of protein katabolism, and if a dog be fed benzoic acid he will excrete, *via* the kidneys, hippuric acid, which is a combination of the benzoic acid and glycocoll. This indicates that the glycocoll must have been furnished by the system. That it was furnished for this particular purpose is not probable. Without much chance of error we may assume that the glycocoll used by the dog's liver in the above-mentioned case was present as a normal constituent of the blood, and that had not the benzoic acid from the portal circulation been brought into relation with the glycocoll it would have been katabolized *in the liver* to the urea plane, either directly or indirectly. This is confirmed by the observation that when the glycocoll is fed to a dog it appears in the urine as urea—having been changed *in the liver*.

Urea is formed in all the metabolic tissues—muscles, glands, and nervous tissues—but by far the greater part is formed in the liver. Some urea results from cleavages and some is built up from CO_2, H_2O, and NH_3.

We may thus summarize: (*a*) As to the PLACE where the protein metabolism takes place: (I) *The early steps* in protein katabolism take place in the various metabolic tissues, principally the muscles, though the alimentary tract is the scene of certain preliminary changes and some changes may be wrought in the blood itself. (II) *The final steps* of protein katabolism take place in the liver.

(β) As to the general CHARACTER of the changes: (I) The complex protein molecule is split up (katabolized) from the plane of living protoplasm either under the influence of living protoplasm or of some of its enzymes. (II) The products of the katabolism are: kreatin, leucin, glycocoll and other amido-acids, sarcolactic acid, ammonium lactate, succinic acid, arginin, cystin, cystein, and other substances are all called midproducts of protein katabolism. (III) These midproducts are further split up or synthesized in the liver to produce urea, uric acid, sulphates, phosphates, etc.

4. The Nutritive Value of Proteins.—Preliminary to a discussion of this topic it will be necessary to define two expressions which have much significance in physiology.

(*a*) **Nitrogen Equilibrium** is an expression signifying the *balance* of *nitrogen* INCOME and OUTGO. It means that the nitrogen which the body loses in the excreta—principally in the urea in man—is just covered by the nitrogen received in the protein foods. If the excreted nitrogen is in excess of the ingested nitrogen it must be evident that the excess must have come from the nitrogen supply of the system. For a very short time this excess might be furnished by katabolism of energy-producing proteins. But at longest a few days would suffice to expend all the available reserve of protein in blood, lymph plasma, and tissue plasma; and the excess would then be drawn from the living active cells of muscles, glands, and nervous system. The organism gives up this life balance very reluctantly and under such circumstances the protein excretion is reduced to a minimum. On the other hand, when the ingested nitrogen is in excess of the excreted nitrogen the balance is in favor of the organism. It might at first be expected that the system would guard this credit very carefully. and store it away in increased volume of living tissue—*e. g.*, increased muscle tissue, increased gland tissue, and increased nerve tissue. Under two conditions and under definite limitations this may be true. First, the growing animal utilizes a part of the nitrogenous balance to build up new tissues. Second, after a period of starvation—negative nitrogen balance—the emaciated living tissues will utilize a large part of the positive nitrogen balance, when the tide turns, to build up and reconstruct the wasted tissues. In both of these cases, however, when the normal growth or condition is reached an excess is not utilized to build up more muscle or more brain, but the system uses it day by day in *increased protein metabolism*, thus balancing increased income by increased excretion. *The normal animal with a sufficient diet maintains a nitrogen equilibrium.*

(*b*) **Carbon Equilibrium** signifies a balance of income and outgo of carbon in food and excretions. Excess of carbon against the organism is an index of a draft on carbonaceous tissue. All tissues are carbonaceous, but not all tissues are necessarily drawn upon to furnish the carbon for increased katabolism. The carbon reserve in the deposited fats usually furnishes the balance. On the other hand a carbon balance in favor of the system is usually deposited as fat. A negative nitrogen balance may exist at the same time that there is a positive carbon balance. Under such circumstances the animal might increase in weight at the same time that its muscle tissues are wasting through lack of sufficient protein. A positive nitrogen balance and a negative carbon balance may exist together and yet the animal may increase in weight.

(c) **The Nutritive Value of Proteins.**—In order to determine the relation of proteins to the general nutrition physiologists have found it necessary to institute two experiments: first, deprive the animal of the foodstuff in question; second, furnish the animal with no other than the one under consideration, meantime watching the progress of metabolism. This method, though open to the objection that so radical a change may not leave the animal in a really normal condition, has yielded some very important results. Pettenkoffer and Voit kept a 30-kilogram dog in nitrogen and carbon equilibrium on 1500 grams of lean meat per day. By increasing the amount to 2500 grams per day the animal maintained nitrogen equilibrium and laid on fat. Pflüger kept a dog in weight equilibrium for a period of eight months on a lean-meat diet. That the weight remained the same for so long a period is sufficient proof that the nitrogen equilibrium and the carbon equilibrium were both maintained. These experiments demonstrate that the carnivorous animal may get all of its required tissue material and energy-producing material from a pure protein diet. Just how far this could be shown to hold for omnivorous or herbivorous animals has not been determined. There is no reason to doubt that if the protein could be presented in a palatable form the results would be practically the same in these animals as in the carnivora. One may safely assume, then, that ingested protein may be used by the system: (I) in a series of katabolic processes which liberate immediately the energy for the life processes; (II) as the nitrogenous factor in the building up of protoplasm; (III) as the carbon and hydrogen factors in the formation of fat. The term protein as here used is intended to include all nitrogenous foods.

One class of proteins—the albuminoids—does not conform completely to the statement just made for proteins in general. The albuminoids, of which gelatin is an example, cannot be built up into living cell protoplasm. Experiment shows that an animal will die about as quickly when kept on a carbohydrate, fat, and gelatin diet as when kept on a carbohydrate and fat diet. The gelatin can be immediately oxidized and may be substituted for a part of carbohydrate or fat, but it cannot be built up into living protoplasm. In other words, the albuminoids seem to be able to play the role of energy-producing proteins, but not of tissue-forming proteins. The relation of the albuminoids to nutrition seems to be in harmony with the hypothesis that only a part of the nitrogenous food is actually built up into living protoplasm, while the rest is katabolized from the protein level, direct. This is, in fact, one of the strongest confirmatory considerations and amounts almost to a demonstration of the tenability of the hypothesis. In summing up ae may say that *the proteins furnish the material necessary* (I) *for* ie *rebuilding of cell protoplasm;* (II) *for direct nitrogenous katabolism;* II) *for deposit as reserve fat.*

5. **The Laws of Nitrogen Equilibrium.**—When an animal receives scanty supply of protein in a mixed diet the organism economizes s tissue protein as well as its energy-forming protein by using arbohydrates and fats for energy production, even if need be drawing pon the reserve fat of the system for this purpose. There is a certain inimum beyond which the protein cannot be reduced without isturbing nitrogen equilibrium, for there is always some katabolism f living protoplasm, and if the organism is not receiving protein ıfficient in quantity and proper in quality to replace this waste iere will be more nitrogen egested than ingested.

When an animal receives an abundant supply of protein in a ixed diet the organism seems to katabolize the usual amount of ssue protein and to draw freely upon the energy-producing protein r the production of energy. If the quantity of carbohydrates and t is sufficient to admit of it, a portion of the food supply is stored fat. Whether this stored fat comes from ingested fat, from carbohyrates, or from proteins is a matter still in controversy. In either case ie protein is so far katabolized as to release the nitrogen, which amediately finds its way to the egesta as urea or related nitrogenous ccreta. From this it appears that with small nitrogenous ingestion iere is small nitrogenous egestion, while with abundant nitrogenous igestion there is correspondingly increased nitrogenous egestion. In eneral, then:

LAW I. *The katabolism of proteins varies with the supply of roteins,* nitrogenous equilibrium being maintained within comparavely wide limits of supply.

LAW II. *The katabolism of protein is nearly independent of uscular work.*

(*a*) LIEBIG'S THEORY.—Liebig believed: (I) that all assimilated rotein is built up into living protoplasmic tissues; (II) that every anifestation of life—muscular contractions, secretion, thought— the result of a breaking down of living tissues; (III) that this katolism of protoplasm releases nitrogen or nitrogen compounds, which d their way more or less directly to the excreta; and (IV) that the antity of nitrogen in the excreta is a measure of the katabolic activity. his theory is so reasonable that it stood unassailed for a considerle period. If it is in harmony with the facts of nutrition one would pect a marked variation of the quantity of nitrogen elimination llowing muscular work.

(*β*) EXPERIMENTS OF FICK AND WISLICENUS.—These two young en, who later attained world-wide renown and recognition as ysiologist and chemist, respectively, put Liebig's theory to a practil test. After using a non-nitrogenous diet for a period of seventeen hours, they began the ascent of the Faulhorn, whose summit they reached after eight hours of the most fatiguing muscular exertion, having lifted their bodies through a vertical distance of 1956 metres. Fick weighed 66 kilograms, he had performed 129,096 kilogram-metres of work in climbing, meantime the heart and respiratory muscles had performed work which was estimated to amount to about 30,000 kilogram-metres, making a total of 160,000 kilogram-metres of energy of muscular contraction. During the climb and six hours subsequent to it the non-nitrogenous diet was continued. During the whole observation period of thirty-one hours the renal excretion was periodically taken and kept for analysis. If Liebig's theory were tenable, then the nitrogen excretion during and subsequent to the climb should have been much increased because muscle katabolism was much increased. But analysis showed *no essential increase of the nitrogen elimination.*

The result of this experiment was generally accepted as conclusive that the Liebig theory is untenable. Voit and Pettenhoffer subjected a dog to alternating days of rest and hard work in a treadmill. The chemical analysis of the excreta showed that the nitrogen metabolism is practically the same on work days as on rest days. The experimenters then made a similar test upon a man, who alternated rest with work in a respiratory chamber. It was found that *nitrogen excretion*, and, therefore, protein katabolism, *is practically independent* of *muscular work.*

Care has been taken not to leave the impression that protein metabolism is independent of katabolism in muscle tissue; katabolism in muscle tissue progresses while the muscles are at perfect rest—*i. e.*, while no contractions are occurring. This *rest katabolism* of muscle tissue liberates heat energy. This process involves the activity of living muscle protoplasm, and there is no reason to doubt that incident to this heat production and incident to contraction a certain amount of living protoplasm is katabolized, and this certain amount seems to be practically the same whether the muscle protoplasm expresses its energy in the form of mechanical work or in the form of heat. In either case the muscle cells seem to be able to utilize absorbed dextrose and the energy producing proteins in this energy liberation. Whether the liberated energy is in the form of heat energy or of mechanical energy, the carbohydrates can be used as well as the circulating protein, so that with sufficient and uniform food there will be nearly a uniform nitrogen excretion, any variations being independent of the variations of mechanical energy liberated.

c. Fats.

1. **Absorption Form.**—Fats are absorbed in the form in which the digestive processes leave them—named in the order of their

quantities: (I) fatty acids and glycerol, (II) soaps, and aulsions (?).

irculation Form.—One would seek in vain for either fatty ycerol, or soap in the portal system as well as in the lacteals. acid be fed to a dog it will appear in the lacteals as fat in m. To *absorbed fatty acid glycerol is joined* to make a fat enters the lacteals in minute subdivision—an emulsion. There to be no doubt that a part, perhaps a large part of the fat is d in the form of soaps—sodium palmitate, sodium stearate, ium lactate. This absorbed soap is decomposed into its nds in the epithelium of the villi. The fatty acid is joined erol to make a neutral fat, which appears in the form of globules in the epithelium. The sodium is joined to water rbon dioxide and may pass into the circulation or it may be l again to bring in another fatty acid molecule. It is claimed e that emulsions may be absorbed as such.

tever the condition in which fat is absorbed it passes into the in the form of an emulsion, which is emptied by the thoracic to the general circulation.

etabolism of Fats.—The fat of each species of animal possesses cular proportion of the three components: Palmitin, Stearin, ein. If a dog be fed on lean meat plus palmitin plus olein cient quantities he will lay on fat; analysis of this fat will hat it is a typical dog-fat having the usual proportion of From such an experiment one must conclude that the s the power to change either palmitin or olein into stearin, he has the power to form stearin from protein. As above he dog may lay on typical fat on a pure protein diet. It is rtain that the stearin may have been formed from the protein t from other fats, and if the stearin why not the others, also? e anything to prove that all of the fat was not directly kat- d to furnish the immediate source of energy and that protein source of all the deposited fat? No, and such may have been e. Another experiment, however, proves that a foreign fat, l, may be deposited unchanged. If such is the case with a fat, may it not also be true of those varieties of fat found ly in the body of the animal under consideration? This is d to be the case. It is believed that *excess of fat may be ed as reserve.* Regarding that which is katabolized immediately known as to the location of the katabolism. It may be oxidized blood; it is more likely that it is oxidized in the metabolic In any case the end products are CO_2 and H_2O, and these lites are excreted by lungs, skin, and kidneys. In the anabolism y acid and glycerin little energy is made latent. In the kat- of fat to its end products CO_2 and H_2O a relatively large t of energy is liberated. The calorimeter shows that one gram of pure fat or oil will liberate about 9500 calories of energy on oxidation. This is much more than is liberated by the same amount of protein. There are 155 atoms in a molecule of tripalmitin, whose oxidation requires 145 atoms of oxygen. There are 644 atoms in a molecule of albumin whose oxidation requires 431 atoms of oxygen. If the relative amount of oxygen required to be taken as an index of the energy liberated, then the fat would have about 1.5 times the amount of energy represented by the albumin. It has 1.63 times the energy of albumin, which fact is probably due to difference in molecular constitution—*i. e.*, in the relative amounts of CO_2, H_2O, and NH_3 formed on oxidation.

4. **Fat Deposit.**—(I) *From the carbohydrates of the food* (see carbohydrates). (II) *From the proteins of the food.* Protein contains 15 per cent. of nitrogen and 50 per cent. of carbon. Urea contains 46 per cent. of nitrogen and 20 per cent. of carbon.

From this it follows that less than $\frac{1}{7}$ of the carbon of protein will be eliminated with the urea which carries off all the nitrogen. From this carbonaceous residue the organism seems able to build up fat. In an experiment upon a dog which was in nitrogen equilibrium a pure protein food containing 68 grams nitrogen and 250 grams carbon was given. When 67.9 grams of nitrogen had been eliminated only 207 grams of carbon had been eliminated. There was a balance of 43 grams of carbon retained and laid on as fat; 58 grams representing 17 per cent. of the total carbon. (III) *From the fats of the food.* It was formerly supposed that much of the deposited fat came from the ingested fat. It is clear in the light of recent investigation that at most only a small portion of it has this source.

4. THE INTERRELATIONS OF THE FOODSTUFFS.

The following figure affords a graphic illustration of the interrelations which have already been discussed.

FIG. 199

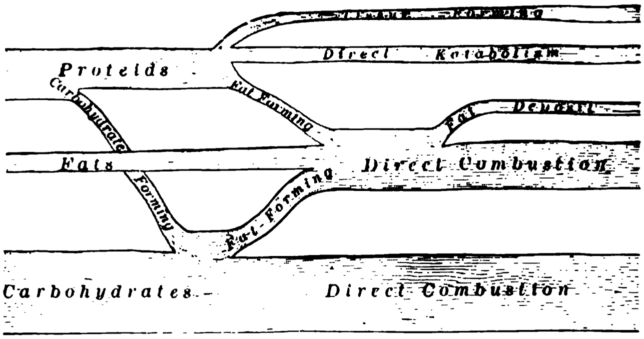


Diagram illustrating the interrelation of the foodstuffs.

B. SUMMARY OF ANABOLISM AND KATABOLISM. 49

a. Anabolism.

Frequent reference has been made to anabolism and many anabolic changes have been given. It is proposed here to enumerate these, explaining such as have not already been discussed.

(I) The synthesis of fatty acids and glycerol in the epithelium of the alimentary tract.

(II) The synthesis of *n* molecules of dextrose with dehydration of same to form glycogen in the liver and in the muscles.

(III) The recombination of peptone molecules into serum albumin and serum globulin in the epithelium of the villi.

(IV) The synthesis of carbohydrates to form fat for deposit in adipose tissue. This process is accompanied by liberation of oxygen.

(V) The anabolism of protein foodstuff or blood proteins into living protoplasm.

(VI) Synthesis of phenol with sulphuric acid. This combination probably takes place in the liver and the resulting phenolsulphate of potassium is excreted by the kidneys.

(VII) Synthesis of benzoic acid with glycocoll to form hippuric acid like the foregoing; this is excreted with the urine.

b. Katabolism.

The cases already discussed will simply be enumerated here.

(I) The hydrolytic cleavage of dextrin molecules by the cells of the intestinal epithelium with the formation of dextrose.

(II) The hydrolytic cleavage of glycogen into *n* molecules of dextrose for each molecule of glycogen. This takes place in the liver and in the muscles.

(III) The formation in metabolic tissues of such midproducts of katabolism as kreatin, tyrosin, glycocoll, sarcolactic acid, ammonium lactate, ammonium carbonate, etc.

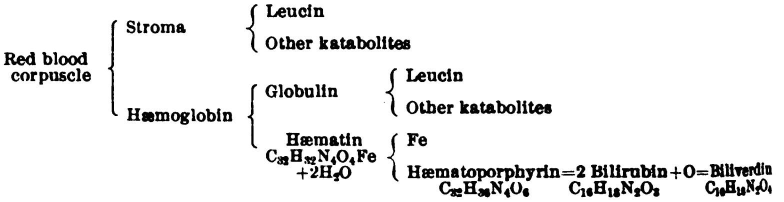
(IV) The formation, in the liver, of such end products of katabolism as urea, CO_2, H_2O.

(V) The katabolism of tyrosin, through a series of oxidation and cleavages from the rather complex paraoxyphenylamidopropionic acid to CO_2, H_2O, and phenol; the latter combining with $HKSO_4$ to form phenolsulphate of potassium, excreted in the urine.

(VI) The katabolism of the red blood corpuscle. The very great importance of the red blood corpuscle, in its relations to the general organism, justifies the discussion of its katabolism at some length, though our knowledge of this process is somewhat fragmentary. The red blood corpuscle has a limited period of activity. At the end of that period the physical union between the hæmoglobin and the stroma of the corpuscle is dissolved.

The "breaking down" of the corpuscle occurs in the liver; it may occur in the red marrow of bones; it occurs also in the spleen. The debris of red blood corpuscles may always be found in the spleen, either in spleen cells or in leukocytes. Whether the senile red blood corpuscle is caught in the spleen pulp and incidentally engulfed by leukocytes or whether it is caught in the general circulation by the leukocytes and brought to the spleen is not known; probably both methods occur.

The following diagram indicates in a general way the steps in the katabolism of the red blood corpuscles:



We may sum up the katabolism of the red blood corpuscles by saying that it is broken up into biliverdin, bilirubin, iron, and a series of such bodies as leucin, which are probably excreted in the form of urea, uric acid, or allied bodies. Notice that some of the decompositions are effected through oxidation and some through hydrolysis. Bilirubin and biliverdin are normally excreted by the liver. How do the products of the first steps in the decomposition make their way from the spleen to the liver? It has been demonstrated by Socin and many others that blood plasma which is free from corpuscles is also free from iron. Then the hæmoglobin does not pass from the spleen to the liver dissolved in the plasma. Lymph which is free from red corpuscles is also free from iron. We are forced to the conclusion that hæmoglobin is carried from the spleen to the liver by *white blood corpuscles.* Many observers have seen liver leukocytes filled with minute particles of matter which, when properly treated, give a microchemical reaction of iron. This is confirmatory of the above conclusion.

The liver will continue to secrete bile, and as a part of the bile bilirubin and biliverdin, after the spleen is extirpated. It is evident, then, that the spleen is not the only place where the first steps of red blood corpuscle katabolism may occur. Possibly it occurs *normally* in the spleen and is taken up vicariously by liver or red bone-marrow after the extirpation of the spleen. Most important to note is the fact that *iron, which is the most difficult of metals to assimilate,* is, early in the katabolic process, split off and, for the most part, *retained in the system.*

C. THE INCOME OF ENERGY.

The income of energy is represented by the potential chemical energy of the food absorbed. To determine the amount of energy income it is first necessary to determine the potential energy of foodstuffs and, second, to determine the amount of foodstuff absorbed. The first step to take in dealing with either matter or energy is to establish units by which these things may be measured.

The calorie is that amount of heat required to raise 1 gram of water 1° C. The large calorie, or kilogram-calorie, is that amount of heat required to raise 1 kilogram of water 1° C.; 1 kilogram-calorie would raise 500 grams of water 2° C., or 100 grams 10° C.

Specific heat is the amount of heat required to raise the temperature of a given body 1° C. Water being the standard, the specific heat of the animal body is 0.8.

Quantity of heat in a body = Wt. × Sp. H. × t., *e.g.*, of a 10-kilo. dog at 38° C. = 10 × 0.8 × 38 = 304 kilogram-calories.

Loss or gain of heat in a body = Wt. × Sp. H. × (T° — t°). How much heat is lost from a 10-kilo. animal cooling from 37.5° C. to 25° C. Loss = 10 × 0.8 × 12.5 = 100 large calories.

Calorimetry is a term applied to the determination of heat units or calories dissipated by any body. The determination is made through the agency of the calorimeter.

The *calorimeter* has undergone many variations since first devised by Lavoisier and La Place in 1780. The first calorimeter—the ice calorimeter—was arranged with a double jacket of ice. The body whose heat radiation was to be determined was placed in a cage within the inner ice jacket. The amount of ice melted by the radiated heat gave an index of the amount of heat given off.

The *water* calorimeter of Crawford (1788) was similarly arranged except that the heat was received by a water jacket and the rise in temperature of the water indicated the amount of heat given off.

The *air calorimeter*, first used by Scharling (1849), has been found more reliable than either of the earlier forms. In its best form as used by Haldane, White, and Washburn,[1] it consists of an animal chamber or combustion chamber and a control chamber (1 and 2, Fig. 200). The body whose heat is to be determined is put into cage 1. In the control cage (2) hydrogen is burned in quantity sufficient to keep the mercury manometer balanced. The number of c.c. of hydrogen burned in an experiment is observed. The calories (gram-calories) produced by 1 c.c. of hydrogen are known. Thus the gram-calories given off by the body to be tested becomes known. Through the aid of the calorimeter one may determine not only the heat given off by the combustion of any oxidizable material (carbon, hydrogen, alcohol, fat, starch, albumin, etc.), but also the amount radiated or conducted away from any body—*e. g.*, a living animal. With the means at hand to determine the potential energy of foodstuffs and the liberated and expended energy resulting from the katabolism of the food it is possible to test the law of the *conservation* of *energy* as applied to the animal organism, and to ascertain whether or not it may be verified in living organisms as in the realm of physical science. The first step to be taken is the determination of the potential energy of the different classes of foodstuffs.

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[1] British Medical Journal, London, 1897, vol. ii. p. 11. Cited by Schafer.

FIG. 200

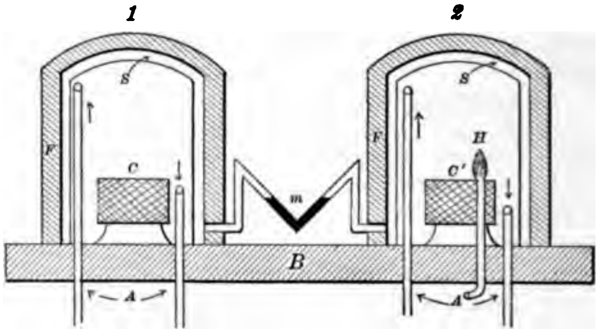

Diagram of air calorimeter: *B*, base; *F*, layer of felt; *C*, cage; *A*, ventilation tubes; *S*, air space; *M*, mercury manometer; *H*, hydrogen flame. (After Haldane, White, and Washburn.)

1. THE POTENTIAL ENERGY REPRESENTED BY FOODSTUFFS.

It is customary to use one heat equivalent for carbohydrates, one for proteins, and one for fats. The value used is an assumed one. The following table gives the calories represented in different foods and other substances involved in nutrition:

SUBSTANCE (1 GM. DRY).	HEAT OF COMBUSTION.	SUBSTANCE (1 GM. DRY).	HEAT OF COMBUSTION.
Starch or glycogen	4182 calories.	Lean beef	5656 calories.
Cane-sugar	4176 "	Casein	5849 "
Dextrose	3940 "	Vegetable proteins	5500 "
Lactose	4162 "	Proteins	5750 "
Carbohydrates	**4180** "	Urea	2528 "
Fat	9686 "	Protein unavailable energy	1650 "
Fat	9423 "	**Protein available energy**	**4100** "
Butter	7264 "	Carbon per gram	8080 "
Fats	**9400** "	Hydrogen per gram	34662 "
Egg, white, 4896 " yolk, 6460	5678 "		

Note that value assumed for carbohydrates is not the arithmetical average, though it approximates an average. In computing the energy represented by a particular menu, one deals with several carbohydrates in various proportions. Instead of computing the different carbohydrates separately it is customary to use the assumed value and to multiply the amount of all carbohydrates by that factor. The other foodstuffs are treated similarly.

2. THE POTENTIAL ENERGY OF COMMON FOODS.

To determine the energy which any food represents it is only necessary to find by analysis the amount of protein, of fat, and of carbohydrate which the food contains, and to multiply these amounts by the factors given in the table of energy of foodstuffs. For example: Oatmeal contains 7.6 per cent. of H_2O, 15.1 per cent. protein, 7.1 per cent. fat, 68.2 per cent. carbohydrate, and 2 per cent. salts. One hundred grams of oatmeal represent in energy:

From protein	15.1 × 4100 cal. =	61,910
From fat	77.1 × 9400 " =	66,740
From carbohydrate	68.2 × 4180 " =	285,076
Total		413,726

The energy of one pound of oatmeal is obtained by multiplying this by 4.5. The following table gives the energy value of a few common foods:

Food (market condition).	Calories per 100 gms.	Calories per pound.
Wheat Bread	286,304	1,301,241
Oatmeal	412,216	1,878,709
Cornmeal	367,428	1,670,866
Beans or Peas	358,656	1,630,091
Potatoes	84,162	382,516
Milk	56,944	258,810 [pt. 291,000]
Eggs	146,736 (2 eggs)	666,915 [doz. 880,416]
Beef	114,900	522,220
Bacon	434,400	1,974,348

3. PRINCIPLES OF DIETETICS.

A brief presentation of some of the principles of dietetics naturally follows the subjects of digestion and metabolism.

Dietetics may be defined as the *science and art of the choice and preparation of food.*

The science of dietetics includes so much of *physiology* as pertains to the nutritional value of the various foodstuffs and foods, so much of *hygiene* as pertains to the influence of foods on the normal individual, and so much of *therapeutics* as pertains to the influence of foods upon the unhealthy individual.

The art of dietetics consists in the skill which is manifested in the choice and preparation of food, which skill is measured by the adaptability of the prepared food to the needs of the individuals to whom it is to be served.

a. An Ideal Ration for an Average Man at Light Work.

The ration given in the following table was arranged by Mrs. E. H. Richards, and is given by Thompson in his practical dietetics.

Materials.	Amount.		Protein.		Fat.		Carbohydrate.		Calories.
	Gms	Oz.	Gms.	Oz.	Gms.	Oz.	Gms.	Oz.	
Bread . . .	453.6	16	31.75	1.12	2.26	0.08	257.28	9.04	1,226,949
Meat . .	226.8	8	34.02	1.20	11.34	0.40	......	......	246,074
Oysters . . .	226.8	8	12.52	0.44	2.04	0.07	....	......	70,508
Cocoa . . .	28.3	1	6.60	0.23	7.50	0.26	9.60	0.34	137,686
Milk	113.2	4	3.63	0.13	4.42	0.16	4.88	0.17	76,829
Broth . . .	456.6	16	18.14	0.64	18.14	0.64	90.72	3.20	624,099
Sugar . . .	28.3	1	....	......	....	......	27.36	0.96	114,264
Butter . . .	14.17	½	0.14	......	12.27	0.50	....	......	115,912
Totals . .	....	....	106.8	......	57.97	......	389.81	......	2,612,323

b. Rations for Average Men under Different Conditions.

The diet should vary with the requirements of the system. The ration which is adequate for a dry-goods clerk would be totally inadequate for a lumberman in the northern forests. One does light work in a warm room; the other does heavy work out-of-doors in the coldest weather. The ration suggested under *a* would be proper for an in-door and sedentary occupation.

The following table, compiled by Atwater,[1] gives an idea of requirements under various conditions:

Conditions.	Proteins.	Fats.	Carbo-hydrates.	Energy in Calories.
Man at light in-door work	110	60	390	2,645,200
" " out-of-door work	110	100	400	3,063,000
" moderate out-of-door work . . .	125	125	450	3,568,500
" hard " " . . .	150	150	500	4,120,000
" very hard out-of-door work in winter .	180	200	600	5,026,000
United States Army rations	120	161	454	3,863,000
" " Navy "	143	184	520	5,012,300
College football team	181	292	557	5,760,100
Teamsters, marble cutters (Boston) . . .	254	363	826	7,829,400
Laborers of Lombardy (Italy)	82	40	362	2,200,200

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[1] Quoted here from Thompson's Practical Dietetics.

c. Rations Varied for Sex and Age.

(Compiled from Thompson's Practical Dietetics.)

Variations of Sex and Age.	Proteins.	Fats.	Carbohydrates.	Calories Energy.
Children to 1½ years old	28 20–36	37 30–45	75 60–90	769,800
Children 1½ to 6 years old	55 36–70	40 35–48	200 90–250	1,423,500
Children 6 to 15 years old	75 70–80	43 37–50	325 250–400	2,048,500
Women with light exercise (Atwater)	80	80	300	2,308,000
Women of moderate work (Voit)	92	44	400	2,435,200
Aged women	80	50	260	1,867,000
Aged men	100	68	350	2,487,000
Sewing girl, London, 93c. per week	53	33	316	1,825,300
Factory girl, Leipzig, $1.21 per week	52	53	301	1,945,200

d. To Arrange a Menu for Particular Conditions.

If, for example, one wishes to arrange a winter diet for a student whose age is twenty-four years, weight 70 kilograms, who is warmly clad, and who takes a moderate amount of light exercise in the open air, he would choose a diet which represents about 3,000,000 calories of energy. If the subject does not crave fat, the carbohydrates must predominate as energy producers. Take, say, proteins 125 grams, fat 90 grams, and carbohydrates sufficient to bring the calories to 3,000,000—*i. e.*, carbohydrates 395.7. With the help of such tables of food analyses as are given above under foods (p. 318 *et seq.*) one can choose a variety and still keep the several foodstuffs approximately as suggested.

e. The Isodynamic Equivalents of Foodstuffs.

In making up dietaries one must frequently take into account the fact that fat may replace carbohydrates or *vice versa*, and that protein may replace either. This interrelation of the foods in nutrition necessitates the use of certain coefficients called isodynamic equivalents.

The isodynamic equivalent may be expressed thus:

(I) Of protein to fat: $\delta\left(\frac{p}{f}\right) = \frac{4100}{9400} = 0.436.$

(II) Of protein to carbohydrate: $\delta\left(\frac{p}{c}\right) = \frac{4100}{4180} = 0.98.$

(III) Of carbohydrate to fat: $\delta\left(\frac{c}{f}\right) = \frac{4180}{9400} = 0.445.$

With the aid of these coefficients one may readily compute the amount of one food to be substituted for another when a change of proportion is indicated. Suppose one wishes to modify the "light-work menu" given above by substituting fats for the carbohydrates in excess of 350 grams, 389.84 — 350 = 39.84 grams. How much fat is equivalent to 39.84 grams of carbohydrates? $\delta \left(\frac{c}{f}\right) = 0.445$. 3984 × 0.445 = 17.73 grams of fat; 57.97 + 17.73 = 75.7 grams fat. The modified "light-work menu" now consists of proteins, 106.8; fat, 75.7; carbohydrates, 350; *but it represents the same energy as before;* it is isodynamic with the menu as tabulated. It may be said here that *the protein should never fall below* 100 *grams per day for an adult man, or* 80 *grams per day for an adult woman.*

D. THE LIBERATION OF ENERGY.

a. The Primary Liberation of the Potential Energy of the Organism.

The potential chemical energy of the tissues and fluids of the body represents the capital of the organism. But this energy must be liberated—must be made kinetic—in order to figure in the life processes of the organism. In the calorimeter the energy of the foodstuffs is liberated by a process of rapid oxidation or combustion. In the animal organism the energy is liberated by a process of slow oxidation usually associated with step-by-step katabolism. It has been demonstrated that the heat is produced in the same aggregate quantity, whether the katabolism or oxidation be slow or rapid. The heat energy determined by the calorimeter, then, will be actually liberated in the organism; and if a man has a daily energy income of 3,000,000 calories and is in a condition of material equilibrium, 3,000,000 calories of energy must be daily liberated and expended.

If the question arises, By what process or processes is the energy liberated? the answer is, briefly: The processes of katabolism are the processes of energy liberation. The two processes are inseparable because in a sense identical.

In what form and in what location is the energy liberated?

It has been intimated that all of the energy is liberated in two general forms and in three locations: (I) in the form of heat and mechanical motion in the muscles; (II) as heat in the active glands; (III) as heat and something analogous to electricity—nervous energy—in the central nervous system: and that the proportions of the total energy liberated in the several locations respectively are approximately as 16 : 3 : 1, or 80 per cent. : 15 per cent. : 5 per cent.

b. The Transformation of Energy.

Much of the energy liberated as energy of motion is converted into heat before leaving the body. This transformation occurs by virtue of friction of the tissues and fluids. As an extreme example let us take the energy of the systole of the heart, which will sum up to a prodigious amount during twenty-four hours. The immense sum of energy is all liberated as energy of motion, but all except an infinitesimal amount is transformed by friction of blood on walls of vessels to heat and leaves the body in that form. If the work done by the heart of the adult at each contraction is 320 gram-metres, and if the heart beats about 72 times per minute, then the work of the heart would amount to 77,970 calories in twenty-four hours (425.5 gram-metres = 1 gram-calorie), or about $\frac{1}{38}$ of the total energy usually expended, or about $\frac{5}{83}$ of a heavy day's work. Nervous energy is also transformed to heat energy.

c. The Conservation of Energy.

The law of the conservation of energy holds as absolute sway in the animal organism as in the non-living world about us. Every calorie of energy taken in either remains as stored-up potential energy, or it escapes from the body in the form of heat, of mechanical motion, or, as in case of urea, as unliberated potential energy. The unliberated energy is, however, corrected in the above and subsequent calculations. Rubner[1] has been successful in practically demonstrating that in the animal body the law of the conservation of energy holds good. The subject of his experiment was a 12-kilogram dog which was confined in a calorimeter cage, thus confining the energy liberated to heat energy. The dog received during the period 228.06 grams of protein and 340.4 grams of fat. This food represented a total of 4,111,970 calories. The amount of heat actually given off during this period, as shown by the calorimeter was 3,958,000 calories. Thus, 96 per cent. of the energy received as potential energy of food appeared as kinetic heat energy. The remaining 4 per cent. may represent the mechanical energy of the movements made in eating the food or other movements made even in a confined space. In another experiment the net energy received in the ingesta was 278,500 calories; the heat energy given off 276,800; in this case over 99.3 per cent. of the energy was given off as heat, leaving less than 0.7 per cent. for mechanical energy.

d. The Expenditure of the Kinetic Energy of the Organism.

All of the kinetic energy of the body is finally expended in one or the other two forms: as *heat*, or as *motion*. A certain amount of energy which enters the system as potential energy leaves as potential energy. The matter holding this energy is urea, uric acid, feces, milk, the reproductive products, and the oil secreted by the skin, or other epidermal products which are shed, moulted, or abraded.

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[1] Zeitsch. f. Biol., München, 1904, Bd. xxx., S. 73.

We are now in a position to take an exact account of the income and expenditure of the energy of the organism, and may express the fact that the two amounts are equal through the use of a *Balance Sheet.*

BALANCE SHEET OF ENERGY FOR MAN AT LIGHT WORK.

	INCOME IN CALORIES.	EXPENDITURE IN CALORIES.
Income:		
Proteins: 110 grams @ 4100 calories . . .	451,000	
Fats: 100 " @ 9400 " . . .	940,000	
Carbohydrates: 400 " @ 4180 " . . .	1,672,000	
Expenditure:		
1. Mechanical work, 212,750 kilogram-metres . . [425.5 gram-metres equivalent to calorie.]	....	500,000
2. Heat lost in 2340 grams of excreta . . . . [Cooling from 37° C. to 12° C.: 2340 × 25 calories.]	....	58,500
3. Heat required to warm 13,000 grams of air from 12° C. to 37° C. . . . . . . [Specific heat of air = 0.26 ∴ 13.000 × 25 × 0.26.]	....	84,500
4. Evaporating 330 grams of water from lungs . . [1 gram requires 582 calories.]	....	192.000
5. Evaporating 660 grams of water from the skin .	....	384,000
6. Radiation and conduction from skin about . .	....	1,844,000
	3,063.000	3,063,000

With varying muscular activity and varying external temperature there will be a fluctuation of the credit side of the account. If the balance is against the system the reserved nutrients are called out for an immediate adjustment of the account. Later the reserve is made good by a more liberal diet.

E. ANIMAL HEAT.

a. General Considerations.

The subject of animal heat belongs logically under *liberation of energy*. Many of the things usually discussed under animal heat have already been treated above. The very great importance of certain phases of this subject justifies special emphasis under a separate heading.

From what has preceded it goes without saying that the heat of the animal body is the liberated heat of metabolism. This heat is subject to constant additions through metabolic activity of the tissues and to constant subtractions through radiation or conduction from the surface.

One of the most remarkable mechanisms in the animal body is the heat-regulating apparatus. Through its operation certain animals are able to maintain a fairly constant temperature, whatever the temperature of their surrounding medium may be. Animals thus able to maintain an even temperature in an uneven medium are classified as *Homothermal* (even temperatured), while animals which are not able to maintain an even temperature, but whose temperature varies with that of the surroundings are classified as *Poikilothermal* (varied temperatured). Poikilothermal or "cold-blooded" animals, by virtue of their sluggish metabolism, have a temperature somewhat higher than the medium when the latter has a relatively low temperature; but above a certain point the temperature of the animal falls somewhat below that of the medium. This is well illustrated by the frog. The frog's temperature in water at 2.8° C. is 5.3° C., in water at 20.6° C. is 20.7° C., and in water at 41° C. is 38° C. The poikilothermal animals are the reptiles, amphibia, fishes, and invertebrates.

The homothermal or "warm-blooded" animals include the birds and mammals. The following mean temperatures per rectum have been determined: horse, 37.9° C.; cow, 38.6° C.; sheep, 40.2° C.; dog, 38.6° C.; cat, 38.7° C.; pig, 38.7° C.; rabbit, 39.2° C.; guinea-pig, 38.7° C.; white rat, 38° C.; monkey, 38.4° C.; common fowl, 41.6° C.; duck, 42.1° C.; pigeon, 40.9° C.; whale, 38.8° C.; seal, 38.9° C.; great titmouse (a bird), 44° C. (111° F.); yellow hammer, 43.2° C.

b. Method of Determining the Mean Temperature.

The usual method of determining the temperature of an animal is to insert a mercury thermometer into some enclosed space, holding it in position until the thermometer registers. Various locations are chosen: the mouth, the axilla, the groin, the rectum, and the vagina. The location most usually chosen—the mouth—is the one which is subject to the greatest accidental variations. Observation has shown that the most reliable and unvarying temperature may be gotten by inserting the thermometer several centimetres (3 to 6 cm.) into the rectum or vagina.

The thermometer should register tenths of a degree. The temperatures recorded above are in the Centigrade scale, in which the difference in the stand of the mercury column at freezing and at boiling is divided into 100 parts or *degrees Centigrade.* The Fahrenheit scale, most used in America, differs from the Centigrade in arbitrarily assuming for the freezing point + 32° and for the boiling point + 212°, dividing the space between these two points into 180° F.; 1° F. is equal to $\frac{5}{9}$° C., or 0.555° C., while 1° C. = 1.8° F. To reduce a Centigrade reading to Fahrenheit it is only necessary to multiply by 1.8 and add 32°—*i. e.*, 38° C. = [38 × 1.8 + 32] 100.4° F.

To reduce a Fahrenheit reading to Centigrade one subtracts 32° and multiplies by 0.555; thus 100.4° F. (100.4 — 32° = 68.4 × 0.555 = 38° C.

From what will follow it will be evident that *in the collection of data for comparison, uniformity of method must be observed throughout a series of observations.* If one wishes to determine the mean rectal temperature in the human subject he should make the observations at a particular time in the day, otherwise his results will be varied by two factors. If he wishes to compare oral with rectal temperature he should observe, as indicated above, every precaution to eliminate every other variable except the one whose value he wishes to determine. If he attempts to compare the morning rectal temperature of a man with the evening oral temperature of a child his results will be valueless.

c. Factors which Cause Variations of Temperature.

1. **Climate.**—There is very little difference in the body temperature of the races inhabiting frigid, temperate, and torrid zones; but if a native of the frigid zone travels into the torrid zone his temperature will rise several tenths of a degree higher than the normal, for the reason that his organs of heat regulation cannot easily adjust themselves to so profound a change in the environment, and the heat accumulates in the body. When, on the other hand, a native of the torrid zone is subjected to a frigid temperature, his heat production cannot keep pace with the heat expenditure and his temperature falls slightly below the normal.

2. **Sex.**—Sex exerts little influence. Extended observations have determined that the temperature of a bitch is 0.2° C. lower than that of a dog, that the temperature of a female duck is 0.3° C. higher than that of the male duck, and that the temperature of the mare is 0.4° C. higher than that of the stallion. This difference is small and inconsistent. The results for the human subjects are contradictory, but the temperature of the woman seems to be subject to greater normal variations than does that of the man.

3. **Age.**—Infants and children have a mean temperature higher than the mean temperature of the adult by about 0.4° C. After puberty the temperature reaches the level of the adult temperature, which level it maintains throughout life with possibly a slight rise in rectal temperature with old age.

4. **The Changing Season.**—The oral temperature follows the seasons, being slightly higher in summer, and slightly lower in winter. The rectal temperature is higher in the winter and early spring than at any other time during the year.[1]

Animals have a remarkable resistance to extremes of climatic changes, the body temperature not rising perceptibly when the external rises several degrees Centigrade above the temperature of the blood. On the other hand, animals and men subjected to sudden fall of temperature in winter will maintain an equable temperature.

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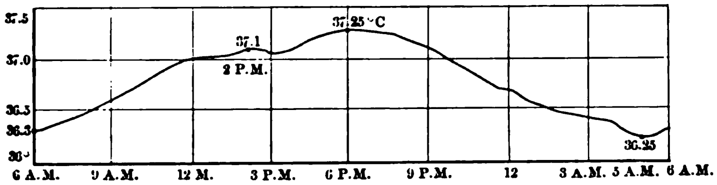
[1] Bosanquet, Lancet, London, 1895, vol. i. p. 672.

5. **The Influence of Day and Night.**—The following chart gives the result of observations by Jürgensen and Liebmeister.[1] Note that the lowest temperature is at 5 A.M., and the highest from 5 P.M. to 7 P.M. The range is just 1° C., or 1.8° F.

FIG. 201



Daily variation of temperature. (After Jürgensen.)

The cause for these variations seems to be the bodily activity of the day and the rest of the night, because in men who work nights and sleep during the day the curve is practically reversed.

6. **Muscular Work.**—The muscles are the heat-producing organs *par excellence*, 80 per cent. of the heat energy of the body being liberated in the muscles. The heat-producing function of the muscles is not by any means independent of their contractility. Just how far these two functions are interdependent is undetermined. It is certain that when an urgent call for more heat is made upon the system the muscles respond with involuntary jerky contractions (*shivering*). The natural impulse is for the animal to begin active voluntary exercise to "warm up." On the other hand, heat is produced in the muscles when they are apparently at perfect rest so far as any visible or sensible contractions are concerned; yet if the muscles are paralyzed by curare they lose their heat-producing power and the animal is at the mercy of external temperature—*i. e.*, potentially a "cold-blooded" animal. There is an increased production of heat during exercise; if the increased amount of heat is not given off from the body as fast as it is liberated within the body there will be a rise of temperature. Repeated observations by numerous observers show that vigorous muscular exercise may be attended by a rise of as much as 1.2° C.

7. **Mental Work.**—For reasons similar to those cited above under *muscular work*, there is a rise of temperature accompanying vigorous mental work. This rise is local and may or may not be communicated in perceptible degree to the system in general, though it is usually con-

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[1] Handbuch der Pathologie und Therapie des Fiebers, Leipzig, 1875.

ceded that the general temperature may rise as much as 0.7° C. with mental work.

8. **Food.**—The increased activity of the digestive glands and of the involuntary muscles of the digestive system causes a somewhat increased production of heat. At the same time a large proportion of blood is collected in the central organ—less upon the surface—and the heat expenditure is increased. These two things, working together, tend to raise the temperature. When other factors tend to lower the temperature a meal would have the effect of keeping up the temperature when it would otherwise fall. This is the effect of a dinner at night.

9. **Sleep.**—Sleep in itself has no influence directly upon temperature. Perfect rest which accompanies sleep causes a slower production of heat and consequently a fall of temperature.

10. **Baths.**—When a warm-blooded animal is immersed in a bath it is at the mercy of two factors, heat production and heat conduction. The first factor is not likely to differ much from the normal; so that the principal factor is the temperature of the bath. If it is above blood temperature the body temperature will rise. If the temperature of the bath is below that of the blood—the usual condition—the temperature will tend to fall, though it must be remembered that the heat-producing factor may in this case be an important one. If the temperature of the bath is much below that of the blood the fall of body temperature may be considerable. A 12-minute bath in sea-water at 6.7° C. caused a fall of oral temperature from 36.7° C. to 34° C.

11. **Extreme Temperatures Artificially Produced.**—When an animal is subjected to extreme heat much in excess of that which it may experience with the changing seasons, it is able to maintain a fairly even temperature for some time *if the heated air be dry*, while in moist heat the temperature quickly rises and death ensues. The reason for this is simple: in dry air the evaporation from the surface keeps the temperature down; while in moist air the evaporation is reduced or quite suspended and the animal has no defence against the extreme high temperature.

When a homothermal animal is subjected to extreme cold the protective process consists in retaining enough of the liberated heat to keep the temperature up to normal. The coat of hair or feathers or subcutaneous fat usually suffices in all animals which are accustomed by nature to low temperature. Animals not so protected succumb soon.

Cold-blooded animals, especially fish, may be cooled to so low a temperature—1° C. to 3° C.—that there is a torpor stimulating death; but with the gradual rise of temperature the life processes start up again.

12. **Drugs.**—*Alcohol*, by increasing cutaneous circulation, causes a fall of temperature.

Chloroform, ether, morphine, chloral, and *nicotine* cause a fall of temperature through decreased heat production.

Curari causes fall through paralysis of the muscles followed by decreased heat production.

Cocaine, atropine, caffeine, and *veratrine* raise the temperature through decreased heat radiation or increased heat production.

13. **Individual Differences of Temperature.**—The mean temperature of individuals of the same species living under exactly the same circumstances will not always be the same. The mean temperature of one man may differ by as much as 0.7° C. from that of another, all conditions being apparently the same.

14. **The Limits of the Variations.**—Pembrey gives the maximum range of normal human temperature as 2° C. (3.6° F.). "By exposure to cold, especially when subjects are victims of alcoholic intoxication, the temperature may fall as low as 24° C. without a fatal issue."[1]

The maximum temperature compatible with life as reported by Wünderlich is 44.75° C. (112.6° F.). Death followed.

d. Temperature Topography.

(*a*) TEMPERATURE OF SUPERFICIAL CAVITIES.
(I) Closed axilla = 37° C. = 98.5° F.
(II) Mouth (under tongue) = 37.2° C. = 97° F.
(III) Rectum = 38° C. = 100.4° F.
(IV) Vagina = 38.2° C. = 100.8° F.

(β) TEMPERATURE OF FLUIDS AND TISSUES.
(I) Blood in left heart = 38.6° C.
(II) Blood in right heart = 38.8° C.
(III) Blood in hepatic vein = 39.7° C.
(IV) Blood in crural vein = 37.2° C.

e. Heat Regulation or Thermotaxis.

1. **Relation of Heat Generation to Heat Expenditure.**—In order to maintain an even temperature of body in a medium of widely varying temperature it is necessary that the organism be provided with some means of adjusting either rate of heat production or the rate of heat radiation. The factors which work together to maintain the *thermotactic condition* are called *thermogenic* and *thermolytic* factors. These two factors have the following relation to thermotaxis: the greater the thermogenesis the higher the temperature; the greater the thermolysis the lower the temperature. These relations may be represented thus:

$$\text{Temperature} = \frac{\text{Thermogenesis}}{\text{Thermolysis}}.$$

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[1] Pembrey's and Schafer's Text-book of Physiology, vol. i. p. 821.

(*a*) **Variation of One Factor.**—From the above expression it is evident that the temperature will be raised by an increase of heat formation or by a decrease of heat radiation.

Furthermore, the temperature may be lowered by a decrease of heat formation or by an increase of heat radiation.

(*b*) **Variation of Both Factors Together.**—(I) *Both of these factors may increase at the same time.* If both are increased proportionally there will be no change in the temperature. If heat formation increases more than heat liberation the temperature will rise. If the heat liberation increases more than the heat formation there will be a fall of temperature.

(II) *The thermotactic factors may both decrease at the same time.* If heat generation is decreased proportionately with heat radiation the temperature would remain unchanged. If heat generation is decreased more than heat radiation there would be a decrease (fall) in temperature. If heat generation is decreased less rapidly than is heat liberation there would be an increase (rise) in temperature.

2. **Thermotactic Centres.** (*a*) **Thermogenic Centres.**—These centres may be classified as *general* and *special:* the former located in the cord, and the latter in the brain. Thermogenic impulses pass from the general spinal centres to the metabolic tissues, probably along the trophic nerves supplying those tissues.

Reflex response to temperature changes outside of the body is accomplished through the action of the special centres located in the brain. These *special centres* are classified as *thermoaugmentor* and *thermoinhibitory*. These centres send their impulses to the general centres and thus influence metabolism only through the general centres and their nerves. The thermoaugmentor centres are located in the caudate, nuclei, pons, and medulla, while the thermoinhibitory centres are located in the region of the sulcus cruciatus and at the junction of the suprasylvian and postsylvian fissures. (Reichert.) The special thermogenic centres are actuated by cutaneous sensory impressions and by sensory impressions from the blood.

(*b*) **Thermolytic Centres.**—The factors of thermolysis are: (I) radiation; (II) evaporation.

Both radiation and evaporation must take place from the surface of the skin or respiratory mucous membranes, principally the former.

Dilatation of the cutaneous arterioles favors both radiation and increased secretion of perspiration. Contraction of the arterioles has the reverse influence upon radiation and evaporation. It then becomes evident that both factors of thermolysis may be increased by cutaneous vasodilatation. The vasomotor centres may be classified as (*a*) vasoconstrictor and (*β*) vasodilator.

(*a*) THE VASOCONSTRICTOR CENTRE is bilateral and is located in the anterior end of the floor of the fourth ventricle. This centre is always in action and constant impulses from it to the various vessels auses their *tonus*. This centre seems to be general in its jurisdiction nd various stimuli may, through its action, cause *general* increase r decrease of vasoconstriction, accompanied by general rise or fall f blood pressure.

(β) THE VASODILATOR CENTRES are not centralized in some cir-umscribed part of the brain or cord, but "diffuse"—*i. e.*, small local entres are located intracranially and extracranially along the central nervous axis. The purpose of this becomes evident when we remember that these centres *act locally*, their apparent function being *to ncrease local blood* supply.

There is in some degree an inverse relation between the vessels of the skin and those of deeper parts on reflex stimulation of vasomotor centres. The cutaneous vessels are often dilated while those of the deeper parts are constricted. This fact makes it evident that he whole surface of the skin may flush through vasodilatation, but he blood pressure still kept up by vasoconstriction in the deep-ying tissues.

Evaporation is increased or decreased through the influence of γ) THE SWEAT CENTRE, which is probably located in the medulla, with subsidiary centres located along the spinal cord.

All of these centres (vasomotor and sweat) are stimulated reflexly by the temperature of the medium which comes in contact with he skin. If cold, then the thermogenic centre is stimulated and the metabolic tissues begin a more active katabolism. Meanwhile the eat supply is conserved by a withdrawal of the blood from the eriphery—*i. e.*, vasoconstrictor centre stimulated. Presently the heat ccumulates through conservation and production, and a reaction sets in, expressed by a cutaneous vasodilatation. The blood comes o the surface, warms the skin, and by exposure falls in temperature o the normal.

On the other hand, when the medium is too hot, the sensory nerves in the skin carry impulses to the centres: (I) the thermogenic activity is inhibited; (II) the sweat centre is stimulated, the perspiration pours out upon the skin, and its evaporation cools the body. The interaction of the controlling factors keeps the temperature within about 0.5° C. of the average—*i. e.*, within a range of about 1° C., though under less usual circumstances 2° C.

Various causes may operate to bring about an abnormally high or low temperature, especially the former. This condition, which is a pathologic one, is a symptom incident to many diseases and will be treated in full under Pathology.

PATHOLOGIC PHYSIOLOGY OF METABOLISM.

We have learned that metabolism is not only the special duty of some organs such as the liver, pancreas, etc., but the common function of each and every cell in the body. Moreover, we are convinced of the fact that there exists a vicarious or compensatory sugar, protein, and fat metabolism, making up for shortcomings in the normal action of tissues or organs detailed for this work. In the third place we are led by many gaps in our knowledge concerning the basis of nutrition to admit that we must await further clinical and experimental proofs before we can expect fully to understand the mechanism of these morbid alterations.

From the above it is evident that we cannot, as yet, and in justice to the facts known, associate a certain morbid condition to a certain organ or to certain tissues. In other words, we must not classify as a morbid, clinical, nosologic entity any pathologic disturbance of metabolism. Indeed, we are not as yet beyond surmises in the pathogenesis of every one of the following symptom-complexes. We are, however, constrained, for the sake of descriptive exposition of facts, to divide metabolic troubles into various groups, and, further, to subdivide them into smaller groups. At the same time the reader is cautioned to take a broad view while he is grouping the morbid phenomena furnished by past and present observers.

A. PATHOLOGIC PHYSIOLOGY OF CARBOHYDRATE METABOLISM.

This implies the study of any deviation in the utilization of ingested carbohydrates and of the failure of the system to furnish the required amount of sugar from other food sources than carbohydrates. The former condition refers more to the intercurrent, variously caused glycosurias, the second to persistent hyperglycæmia with hyperglycosuria. Glycosuria, diabetes mellitus, and obesity grow upon the same pathogenic trunk whose branches pursue their individual directions while springing from the same soil. None of these three conditions can be called a clinical entity; they merge into one another at their very source.

1. GLYCOSURIA.

Glycosuria means the presence of an abnormal amount of sugar in the urine. It is usually accompanied by hyperglycæmia or excessive quantity of sugar in the blood. The metabolic organs, including the kidneys, are very sensitive toward any deviation from the normal of the sugar equilibrium of the blood. The renal epithelium cannot retain over 2 per cent. of sugar in the blood plasma.

1. **Etiology and Pathogenesis.**—Generally speaking any functional or organic disturbance of any organ or tissue contributing toward carbohydrate metabolism may produce or at least aggravate glycosuria

(*a*) **Physiologic Glycosuria,** so-called, occurs in certain persons of apparently good health in whom, after the rapid ingestion into a fasting stomach of 100 to 180 gm. of dextrose or of 100 to 125 gm. of levulose, is usually followed within one-half to three hours by the appearance of the same ingested variety of sugar in the urine, which in quantity never exceeds 3 per cent., and stops after four to five hours' duration. This condition is in my opinion, no more physiologic than the so-called physiologic (Leube) or orthostatic (Linossier) or cyclic albuminuria. (See page 535.) It is a condition of sugar metabolism on the border-line of the normal and abnormal, although Van Noorden and others consider it a normal occurrence in some persons. The cause lies in the functional or organic impairment of the capacity of an organ or tissue to utilize, to produce, or to dispose of sugars. We do not know the individual share taken by those structures in sugar metabolism; consequently our notions about pathogenesis must be correspondingly fragmentary.

(*b*) **Toxic Glycosuria** after morphine, chloral, cocaine, and other poisoning or after ether narcoses, etc.

(*c*) **Glycosuria** associated with lesions of the **nervous system** in any of its parts, but especially of injuries to the structures in the floor of the fourth ventricle and of the basal ganglia. This glycosuria is the clinical equivalent of the sugar puncture of Claude Bernard. In sympathetic nerve lesions we also observe it very often; consequently we find it clinically in the following morbid conditions when they occur in persons of at least fair nutrition:

Cranial, especially basal fractures; apoplexy, from any cause; lesions of the cervical sympathetic, as in Graves' disease; organic brain disease—*e. g.*, paralytic dementia, paralysis agitans, etc.

This inherited or acquired deficiency of sugar metabolism appears at such occasions only, and either passes off rapidly or merges sensibly or unnoticeably into permanent glycosuria. The proximity of the nervous lesion to the onset of glycosuria has given rise to the view that this variety is neurogenic in causation (Van Noorden, etc.), but this is not sufficiently proven. A latent glycosuria disposition was prompted to life by the entering upon the scene of a trauma or other pathologic agency.

(*d*) **Glycosuria in Hepatic and Pancreatic Diseases.**—The synergy of the liver and pancreas in general metabolism is well established and recent observers contend from clinical experience (F. C. Ohlmacher) and from animal experiments (Ssoboleff) that the pancreas acts vicariously for the liver in the metabolism of sugars.

Steinhaus goes so far as to describe the occurrence of glycosuria as a bond between the pancreas and the liver, and it is certainly logical to suspect both of these organs in a given case of glycosuria. However, statistics show a greater percentage of glycosuria in pancreatic diseases than in hepatic disorders, occurring in about 25 per cent. to 35 per cent. of all liver diseases, cirrhoses, and in over 50 per cent. of all pancreatic diseases. So-called alimentary glycosuria is a sign of hepatopancreatic insufficiency.

(*e*) **Phloridzin Glycosuria** experimentally produced in dogs (von Mering) comes nearer to diabetes mellitus than any other glycosuria. It is not accompanied by hyperglycæmia, occurs in a well-fed and in a starving animal, and it demonstrates that the kidneys have a certain influence in the production of, or course of, glycosuria and that proteins may become a source of sugar formation.

2. DIABETES MELLITUS.

This morbid condition implies the inability on the part of the organism to husband sugar. It is a glycosuria, which after repeated careful and painstaking examination of the individual affected cannot be ascribed to any recognizable cause. The disturbances of the carbohydrate metabolism are profound and they constitute the most striking symptoms of diabetes; but the percentage of the sugar in the urine is no guide to the severity of the case. The whole organism suffers from probably simultaneous alterations of protein metabolism, although they are not as early recognized. At the present time we cannot incriminate one single organ alone with the causation of essential glycosuria or diabetes mellitus. Even the pancreas, much as we have learned about it in later years, is not to be considered as the exclusive causal factor. There are many cases of diabetes in which glycosuria is the most visible and the first noticed symptom, yet for all that, neither the severest, nor first existing one of that remarkable and enigmatic perversion of metabolism.

Glycosuria and diabetes mellitus very often merge imperceptibly into one another and we recognize them only by the ends or extremities. The clinical division of diabetes mellitus into two varieties, light and severe, is based upon the fact that in the light form only the ingested sugar appears in the urine, while in the severe form even the body sugars or those formed from the proteins appear in the urine. These two varieties are kept separate by Leegen, while Van Noorden and Eschbach consider the distribution an artificial one.

1. **Etiology and Predisposing Causes.**—(I) Hereditary; (II) race; (III) mental exertion, strain, overwork; (IV) mode of living, epicurism; (V) trauma; (VI) neuropathic instability; (VII) causes unknown to us.

2. **Pathogenesis.**—Something causing a disturbance in the synergy of the carbohydrate metabolic tissues, prompting the one or the other to a diminution or cessation in its function. Neither the nervous system nor the liver, nor even the pancreas, has the monopoly of producing a glycosuria. They may act vicariously for the deficiency from one of them without being aware of it until an external event, such as psychic or physical trauma causes an explosion-like manifestation of the hyperglycæmia and glycosuria.

Physiologic chemistry would present to us three ways in which hyperglycæmia and glycosuria occur:[1] (I) Inadequate distribution of carbohydrates in the body (insufficiency of the glycogen reservoirs liver and muscles. (II) Diminution in the property residing in the tissues of seizing upon and breaking up the sugar molecules. (III) Diminution of the property residing in *certain* tissues of converting the sugar molecules into a fat molecule.

3. **Pathologic Physiology of the Symptoms.**—There are two groups of signs: (I) Those arising from the excessive quantity of sugar in the blood. (II) Those arising from the glycosuria—*i. e.*, the symptoms attributable to the elimination of sugar from the blood current to the outer world.

(*a*) **To the Presence of Hyperglycæmia** are due the following symptoms:

(*α*) The loss of heat-producing material to the system; this is a very important defect.

(*β*) Alterations in the tissues caused by the toxic substances not eliminated or generated *de novo* in the metabolic tissues (β-oxybutyric, diacetic acid, and acetone are the best known ones). (I) Nervous symptoms: neuritis, myelitis, parencephalic amblyopia, retinitis, cataract. (II) Psychic symptoms: dementia, senility, aphasia. (III) Cardiovascular symptoms: arteriosclerosis, nephritis, gangrene.

(*γ*) Excessive loss of nitrogen manifested by abnormally high nitrogen content in the urine.

(*δ*) Depression of the resistance to bacterial infection; tuberculous pyogenic germs especially.

(*b*) **Symptoms Incidental** to the presence of sugar in the renal secretion.

(*α*) Subtraction of water from the tissues, (I) polyuria and polikiuria; (II) polydipsia.

(*β*) Those due to irritation of excretory organs or tissues working vicariously; the nephritis, which in time leads to albuminuria; furunculosis, pruritus, eczema, keratosis, etc., the diabetics of Jeanselme.

(*γ*) Abnormal urinary constituents: Sugars, Ammonia, Acids.

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[1] Van Noorden, Twentieth Century Practice, p. 60.

3. DIABETIC COMA.

This peculiar nervous symptom-complex occurs in nearly all cases of diabetes, and in the majority of lethal cases usually closes the scene. It is caused, according to some authors, by a specific toxic substance (Frerichs) unknown as yet, and appearing in the blood of diabetes at such times and upon unknown provocations. Others, however, and apparently with more reason, ascribe the coma and the poisoning to the accumulation of β-oxybutyric, diacetic acids, and other allied substances which are excreted in a quantity directly proportionate to the gravity of the cases. Experiments show that in dogs and cats a typical coma diabeticum can be produced by the injection of β-oxylentyric acid. We must, however, not forget that uræmia may be associated with or may even constitute itself the real cause of the comatose state. The most characteristic symptom of diabetic coma is the dyspnœa or air hunger (Kussmaul), a peculiar form of breathing due to the stimulation of a special centre in the medulla oblongata.

B. DISTURBANCES OF FAT METABOLISM: OBESITY.

This morbid condition forms the connecting link between morbid alterations of sugar metabolism on the one hand and that of fat on the other. Indeed, a very large number of cases of obesity merge into diabetes. It is often very difficult to perceive the dividing line between true obesity and portliness in stout persons who, to all appearance, are in good health.

1. **Etiology.**—There are many causal factors entering into the production of obesity, of which the important ones are: (I) inherited tendency; (II) faulty nutrition; (III) phlegmatic, easy-going, epicurean life; (IV) intercurrent diseases (chlorosis, convalescence from severe diseases), *together* with an hereditary predisposition; (V) alterations in the genital glands and sexual activity also in predisposed persons (normal and premature menopause; alcoholism; diseases of the ovaries, etc.); (VI) certain disturbances of the thyroid gland—*e. g.*, cretinism.

2. **Pathogenesis.**—The disposition of an abnormal amount of adipose substance in the elective fat-regions of the body—*e. g.*, around the heart and kidneys, in the liver, omentum, and panniculus adiposus is the expression of obesity. The adipose material is mainly derived from ingested carbohydrates, but also from ingested fats and proteins. We do not as yet know what agencies preside over the metabolism of fat. It is a remarkable fact that the quantity of fat in the body may vary between 16 to 28 per cent. of the total weight in normal

conditions, while the nitrogen and the water percentage vary only slightly over or under 14 per cent. and 69 per cent. respectively.

3. **Pathologic Physiology.**—Cases of obesity are best divided into three groups: (I) plethoric obesity; (II) anæmic obesity; (III) hydræmic obesity.

a. Plethoric Obesity.

Plethoric obesity is of congenital, hereditary origin, and the individuals afflicted may feel perfectly healthy as long as they live according to good hygienic precepts and until old age sets in. They are mentally and physically very active, although they walk all this time on the dividing line between health and ill health, and in the majority of cases environments lead them to commit imprudences, followed by the usual symptoms of obesity, which are disturbances in the economy from mechanical impediment to the proper function of locomotion, cardiac circulation, bodily and mental exercise, liver metabolism, proper digestion. In these cases we have usually a polycythæmic condition of the blood.

b. Anæmic Obesity.

Anæmic obesity is pathologic from its onset. It seems usually to occur in conditions of malnutrition from such causes as chlorosis, menopause, castration, alcoholism, lactation, etc. Here we have a chloranæmic condition of the blood (Hayem-Malassez). The hereditary factor does not play here the same important role as in the preceding group. It lasts either a number of years, then recedes, or it continues, and with the plethoric variety it merges into hydræmic obesity.

c. Hydræmic Obesity.

Hydræmic obesity derives its name from the abnormal amount of water in the tissue due to deficient heart action on the one hand and to diminished activity on the other. It is very often associated with morbid conditions, causing more or less extensive œdema of the dependent parts of the body as well as of the larger serous cavities.

C. PATHOLOGIC PHYSIOLOGY OF NITROGENOUS METABOLISM.

In this chapter we will briefly review our knowledge upon the disturbances of metabolism accompanying or ensuing upon perversion of one or more of the functions of the metabolic organs, such as the liver and the pancreas. But we regard it as a pedagogic impropriety and as a scientifically inaccurate systemization to inculpate the liver alone in hepatic cirrhosis or the pancreas solely in glycosuria and diabetes mellitus. The above-named morbid conditions are but links in the chain of pathologic events which, perchance, may be localized in one or two organs, yet never exists isolated—*i. e.*, without interfering with the rest of the metabolic processes.

1. HEPATIC INSUFFICIENCY.

By this we understand the failure of one or more of the hepatic functions to take their normal share in metabolism. It is a comprehensive name and well fitted to the multiform duties of the liver which, since it is physiologically called upon to produce a variety of metabolic changes, must also manifest its morbid alterations in various ways. Biliary and glycogenic disturbances are the handles by means of which we have grasped the great crucible of the economy —the liver. But in later years we have learned to use additional means of inquiry into the mechanism of the various hepatic functions. Clinical and experimental observers have made efforts toward the better understanding of the multiplicity of the liver function. As a result we are able to present the inadequacy of the liver to physiologic demands under the head of hepatic insufficiency. This may manifest itself in the following ways:

a. Alimentary Glycosuria.

Alimentary glycosuria, a failure of the liver to hold its sugar, was already foreseen by Claude Bernard. This intolerance is greater toward levulose than toward glucose.[1] It occurs in about 30 per cent. of all liver diseases; but we do not know in how many of these cases the pancreas also is involved. The power of the liver to utilize sugars varies considerably normally, but if glycosuria occurs after 150 to 180 gm. of dextrose and after 100 to 125 gm. of levulose, we are justified in assuming a faulty glycogenic function of the liver.

b. Urobilinuria.

Urobilinuria is an important evidence of liver disturbance as it expresses the failure of the chromopoietic function, as a consequence of which pigments from the normal or excessive hæmolytic processes are defectively eliminated.[2] Hayem calls urobilin the pigment of the diseased liver (Gilbert-Carnot).

c. Hypoazoturia with Ammoniuria.

This expresses the uropoietic disturbances of the liver, and shows a permanent diminution in the urea output, which is nearly always accompanied by excessive ammoniuria. The liver is unable to katabolize proteins to the urea level and allows the NH_4 radicals to be excreted unchanged. The less urea excreted, the more NH_4, as a rule, appears in the urine. As uropoiesis is a specific hepatic function, its permanent disturbance is one of the best signs of liver insufficiency. The exogenic part of uric acid derived from the purin bases as well as the katabolism of NH_4 is diminished.

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[1] H. Strauss, Charité-Annalen, 1903, vol. xxviii. p. 170.

[2] Leube, Klinische Vorlesung, Juliusspital, Würzburg, April 21, 1903.

d. Cyclic Elimination of Crystalloids.

Cyclic elimination of crystalloids, such as chlorides and methylene blue. This is the most constant urochemical evidence of hepatic insufficiency, and it is in direct relation to the gravity of the liver disease.[1] The cyclic elimination of these substances is probably due to the cyclic stimulation of a nervous centre from the simultaneous accumulation in the system of some substance or substances normally rendered harmless by the action of the liver.

e. Disturbances of the Biliary Function.

It is evident that the elaboration of bile should also suffer in proportion to the impairment of other hepatic functions. And in fact we have in such persons an icteroid skin, seborrhœic condition of the cutaneous tissues, frequent headaches, and frequently abnormal accentuation of the normal variations of psychic life—*e. g.*, depression, melancholia, etc.

f. Increased Toxicity of the Urine.

The coefficient of toxicity of the urine, established by Bouchard, is very frequently increased owing to the retention or the elaboration of noxious substances of the liver.

French and Italian investigators are firm believers in the reality of this urochemical evidence, while most of the Germans and Americans flatly deny it. English observers are fairly evenly divided about this matter.

g. Digestive Disturbances.

Digestive disturbances, the effects of continued perversion of one or more of the liver functions, must, of course, react upon the digestive system. The gastrointestinal epithelium suffers by sympathy, and secondarily during every profound metabolic deviation of the liver. And in fact the dyspeptic symptoms usher in the irretrievably progressing hepatic diseases, such as fatty degeneration and the cirrhoses. This ushering in or foreshadowing stage is called hepatism, or the preliminary stage of liver diseases. (Gilbert-Carnot.)

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[1] Achard-Castaigue, Épreuve du bleude methylène, etc., Paris, 1900.

Pancreatic and intestinal digestive secretions suffer more or less in all cases of hepatic insufficiency.

2. PANCREATIC INSUFFICIENCY.

Outside of fat necrosis, which is a rapid autolysis of the organ and of the mesenteric peritoneal fat, with sudden onset and of unknown nature, there is no disease which is distinctly pancreatic. Indeed, R. H. Fitz believes that there is no pathognomonic symptom of pancreatic disturbances. In case of glycosuria we can strongly suspect the pancreas, but never inculpate it alone. Its special and specific glycolytic ferment may be aired in some way without any clinical evidence of it. This organ contributes toward the metabolism of the three food elements, and in addition furnishes an internal glycolytic as well as a rennin ferment. We do not as yet possess any definite urochemical, hæmochemical or histochemical means to make a sure, clinical ante-mortem diagnosis of pancreatic diseases, but the following symptoms should cause us to suspect the presence of some kind of morbid alteration of the organ.

(I) Finding of *ingested muscle fibres* in the constipated stool of an individual who ingested lean meat. This indicates deficiency of the trypsin action. (Fitz.)

(II) Failure to find *carbolic acid* in the urine of an individual to whom salol was given per mouth, this substance as we know being decomposed (35 per cent.) into carbolic acid and (65 per cent.) salicylic acid, which appear as such in the urine. The splitting-off action is the function of the pancreas.

(III) The presence of *glycerin* in the urine after ingestion of fats, which also occurs during deficient pancreatic action. (Cammidge.)

3. ICTERUS.

This is the most striking and, clinically, the most important disturbance of the liver. In fact, the morbid alterations of the bile functions of the liver have up to now served as a basis for the classification of hepatic disorders. This function, unlike the glycometabolic one, varies within wide limits—*e. g.*, the quantity of bile varies from 5 to 1500 c.c. per day. Bile is a complex substance (bile acids, bile pigments, and cholesterin), a product of secretion of elevation. Consequently we find icterus a complex phenomenon, difficult of interpretation in regard to causation, pathogenesis, and symptomatology.

Experimental knowledge has too limited a scope, and it is here where clinicians have furnished us the greater number of facts.

1. **Definition.**—The term icterus applies to a discoloration of the skin of a yellow or yellowish hue. It does not imply what the kind of coloring matter is; it states merely a phenomenon without reference to its origin or variety.

2. **Pathogenesis.**—Icterus is at bottom a diversion of the bile into the lymphatic or venous channels instead of the normal discharge into the intracellular and intercellular biliary capillaries. The exact conditions under which this occurs are not known yet, but we have a umber of theories for the elucidation of the production of icterus.

(*α*) PARAPEDESIS of the bile (Minkowski), the biliary substances assing through the wall of the bile capillaries into the lymphatic r venous channels owing to chemical alterations in composition.

(*β*) MECHANICAL OBSTRUCTION in the biliary channels in any porion of their course, increase of pressure in the bile capillaries, with ubsequent outpouring of bile into the vascular channels.

(*γ*) DISTURBANCE OF THE CHROMOPOIETIC functions of the liver cells nay be due to a variety of causes—*i. e.*, excessive amount of blood igments to be disposed of, diminution in the chromopoietic power f the cells from any cause.

In view of the diversity of pathogenic conditions we can easily ee why there are several varieties of icterus, and yet notwithstanding he variable causations the resulting symptoms are practically of the ame character in every case.

(*a*) **Obstructive or Mechanical Icterus.**—Obstructive or mechanical cterus, the most frequently observed; caused by an obstacle to the utflow of a normally or abnormally elaborated bile. Such obstacles nay be or may not be the result (I) of inflammation, cholangitis, atarrh of common duct, spasm of large bile channels, etc., or (II) he result of simple obstruction (gallstones, biliary concretions, inking of the large ducts, clogging by intestinal worms and obstrucion at or near the papilla of Vater); (III) spasm of the common duct, s in emotional icterus—*e. g.*, after a debauch.

(*b*) **Icterus from Polychromia.**—Icterus from polychromia or excesive accumulation of pigmentary substances resulting from the breaking down of hæmoglobin and normally eliminated in the bile by way f the intestines. We meet with such conditions in pernicious anæmia, malarial troubles or paludism, yellow fever, and in some cases of epticopyæmia, etc. (Leube). It is, as a rule, synonymous with the o-called *toxic icterus*, caused by the ingestion of poisonous substances f animal or vegetable origin, capable of setting free by its noxious ction a large amount of pigment, which is, of course, carried by the phagocytes and other impromptu scavenger cells to the liver for urther modification and elimination. This occurs in snake bites, hloral, phthalin, pyrogallic acid, mushroom poisoning, etc.

(*c*) **Icterus Neonatorum.**—Icterus neonatorum, occurring in over 75 per cent. of all newborn soon after birth, lasting three to seven days, and without any noticeable ill-effects in the majority of cases. It is due (I) to the fact that a part of the portal blood passes around the liver and joins the vena cava directly by way of the ductus Arantii. The blood thus escaping hepatic purification is highly charged with biliary matter of which the meconium contains 1 per cent. and contributes to that striking yellowish discoloration of the infant. (II) There is very active breaking down of nucleated red blood corpuscles during the first days of life which throws an excessive amount of pigments upon the liver, which organ is unable to excrete it with sufficient rapidity.

(*d*) **Policholic Icterus.**—Icterus from policholic (the family cholæmia of Gilbert) occurs in some families of European and mixed Latin races, also Philipinos (Severino). These individuals are in good health otherwise, although they constantly show bile staining of the external surfaces, and the presence of biliary substances in the urine. Policholic icterus undoubtedly exists, although its pathogenesis is not clear.

(*e*) **Urobilin Icterus.**—Urobilin icterus (Gubler, Dreyfuss-Brissac, Stadelmann) is occasionally found in persons affected with some obscure metabolic disease. It may exist and last a long time by itself, and as yet is devoid of a satisfactory pathologic interpretation. Of whatever significance it may be,—it is the expression of disturbed chromogenic function of the liver. In many cases a focus of blood extravasation has been located and then a digestion or katabolism of red blood corpuscles assumed as an explanation of the presence in the blood and urine of an excessive amount of urobilin.

(*f*) **Infectious Icterus.**—Infectious icterus, or Weil's disease, is caused by some unknown pathogenic organism, and the icterus which is one of the main symptoms can as yet not be explained by the theories and facts at our present command. Strictly taken, it is an infectious disease with a selective morbid action upon the liver and particularly upon its chromogenic functions.

4. CHOLELITHIASIS.

This term implies a morbid state of metabolism in general and of the biliary organs in particular, during which there is a formation of concretions within the bile passages. These concretions may originate or keep increasing in any position of the biliary apparatus. Consequently the systemic and local disturbances will greatly vary with the location as well as the size and rapidity of their formation. Cholelithiasis is a very frequent condition in the human being, although in the majority of cases we are unable to diagnosticate it clinically, because, first, there are no symptoms whatever, or, secondly, any signs due to it are so slight, or so masked by other ailments (dyspepsia, movable kidney, etc.), that it is very difficult to recognize them.

1. **Etiology and Pathogenesis.**—These causative factors at work are multiple and their *modus operandi* equally variable. The consensus of view of modern workers, however, is about the following: (I) A diseased condition of the mucous membrane of the gall-bladder and of the biliary passages, leading to an increased formation of cholesterin and of calcium compounds, is the primary cause of gallstone formation. Stasis of the bile ensues, accompanied by greater viscidity and a tendency to form precipitates of bile pigment, calcium, and cholesterin. (II) It is, moreover, very probable that a special, as yet ill-known hereditary or acquired disposition toward disturbances of nitrogenous metabolism is at the bottom of cholelithiasis. Diathetic disorders, such as gout, obesity, etc., are very often accompanied by cholelithiasis or the latter may be their sole substitute.

One by one the various following factors, after a transitory reign of importance, have receded to their natural work of predisposing or contributing causes: (I) Infection, particularly by organism of the bacilli coli groups, and of the bacillus of Eberth. (II) Sedentary habits, epicurean life, faulty diet. (III) Gastroduodenal catarrh. (IV) Intra-abdominal diseases, especially of the right side (appendicitis, movable kidney, etc.).

2. **Pathologic Physiology**—The symptoms begin to manifest themselves in a predisposed individual with the advent of more or less obstruction to the flow of bile, or, oftener still, with the accession of some infection. Again, some great change in the arrangement of the abdominal pressure—*e. g.*, operations, birth of a child, etc.—may wake the latent gallstones into activity.

As said before, we have in icterus a complex intoxication constituted: (I) by the circulation in the blood of bile salts and of bile pigments (headaches, bradycardia, diminished reflexes, ocular disturbances, etc.). (II) By the effects of toxic substances normally eliminated with the bile, or elaborated *de novo* by the morbidly altered hepatic cells (pruritus, furunculosis, deficient coagulation of the blood, even hæmolysis to hæmoglobinuria). (III) By the results of the more or less complete absence of bile from the intestines (loss of ingested fats, 20 to 35 per cent.), increased putrefaction, diminished peristalsis or constipation. (IV) The presence and character of coexisting infection or of an intoxication of some sort—*e. g.*, uræmia—certainly influences more or less profoundly the physiognomy of a given case of icterus, inasmuch as the resulting toxæmia would aggravate or even overshadow the other symptoms.

5. GOUT.

Gout cannot be defined as a disease, but only as one of the manifestations of a peculiar morbid constitution or diathesis. It is not a simple entity, but a local disorder and a general perversion of metabolism and of excretion. We are accustomed to consider it as a morbid syndrome during which there are certain important, probably characteristic, yet ill-known variations of the uric acid in the blood as well as in the urine. These alterations may, or may not, be accompanied by subjective symptoms; in other words, gout may be latent.

1. **Pathogenesis.**—The underlying directly causative factors of gout are unknown, and it is perhaps more profitable not to confine all our attention to their elucidation. It is necessary to await further discoveries in the domain of protein metabolism, especially in the relation of uric acid or allied bodies, to explain the acute or chronic manifestation of what we call gout. The direct causes, thus, being so well hidden from us it is evident that their mode of action can only be surmised. Accumulation of uric acid and allied bodies in the tissues is the probable cause of gouty outbreaks and not excessive formation, as was formerly believed.

2. **Etiology.**—If the pathogenesis of gout is so cloudy as yet, there are certain conditions or influences favoring the production of this diathetic disorder. They are (I) heredity: gout is found in the same family for generations, usually in the articular forms, but occasionally in a visceral form; (II) climate: the temperate zones favor its production; (III) sex: males predominate; (IV) habits and diet: a very important predisposing cause, a sedentary life with epicurean habits in a phlegmatic gentleman, is the best soil for gout; (V) age: gout is a disease of adult years; (VI) season: it manifests its action mainly in fall or spring; (VII) presence of poison or toxins in the body—*e. g.*, of lead or other heavy metals, of alcoholism, etc., facilitate the onset and progress of gout.

3. **Pathologic Physiology.**—In the study of the symptoms of gout we must consider four groups of facts: (I) The gouty, "lithæmic," diathesis, with its visceral and constitutional affiliations. Thus, we must ascertain whether or not this gouty disposition has existed or exists in the individual under some other form—*e. g.*, migraine, asthma, some forms of arthritis, cholelithiasis, etc. For, indeed, the clinical expressions of gout may interchange and may also be associated. (II) The chemistry of the blood and of the urine; outside of the excessive acidity of the urine, and presence of an abnormal amount of uric acid, all other findings are too variable to allow of any final conclusions. (III) The local effects of the precipitation of urates (sodium quadri-urates of Roberts) around the joints, as well

s in other localities—*e. g.*, muscles, liver, connective tissues, etc. 'ery often the manifestations of gout are articular only, or mainly ı young, robust, sthenic individuals, while later on in life the viscera re in the lead of morbid symptoms. (IV) The association of other omatic or nervous disorders—*e. g.*, nephritis, neurasthenia, obesity, enolithiasis, etc.—will modify the physiognomy of gout in its acute s well as chronic, in its latent as well as in its manifest varieties.

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CHAPTER VIII.

EXCRETION: INTRODUCTION.

DEFINITIONS.
GENERAL CONSIDERATIONS.
ANATOMY OF THE KIDNEY.
- *a.* Blood Supply of the Kidney.
- *b.* The Uriniferous Tubules.
- *c.* The Innervation of the Kidney.

THE PHYSIOLOGY OF EXCRETION.

A. RENAL EXCRETION.

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  - (2) *Specific Gravity*
  - (3) *Reaction.*
- *b.* Chemical Composition. Tabulated.
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- *b.* Chemical Composition.
  - (1) *Organic Constituents.*
  - (2) *Inorganic Constituents.*

THE PROCESS OF CUTANEOUS EXCRETION: PERSPIRATION.
- (1) The Influence of the Nervous System upon Cutaneous Excretion.
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D. INTESTINAL EXCRETION.

PATHOLOGIC PHYSIOLOGY OF EXCRETION.

A. RENAL EXCRETION.

1. RENAL INSUFFICIENCY.
2. ALBUMINURIA.
3. EXCRETION OF WATER AND SALTS.
4. ECLAMPSIA.
5. URINARY POISONING.

EXCRETION.

INTRODUCTION.

1. DEFINITIONS.

Excretion.—"The separation of waste products of an organ or of the body as a whole, out of the blood. The material so excreted." (Gould.) Comparison of this definition with that of ***secretion*** (p. 2[illegible]4) shows that excretion is looked upon as a special form of secretion, the distinction being that secretion is elaboration of any product from constituents of blood or lymph, while excretion is the ***separation** of waste products from the blood or lymph.*

Egestion.—"The expulsion of excrements or of excretion." (Gould.)

Egesta.—"(pl. of egestum, fecal matter.) The discharges of the bowels or other emunctory organs." (Gould).

Let us make a specific application of these definitions. The parietal cells of the gastric glands take up NaCl and H_2CO_3, or $CaCl_2$ and Na_2HPO_4 from the blood, where they form normal constituents; and these active cells *elaborate new products*—i. e., *they form a secretion.*

An excretion differs from a typical secretion in that the former represents waste products which escape, from the place where the katabolism occurred, into the lymph or blood and so circulate through the system until brought to some organ whose active cells have the power to *select* and *separate these waste products out of the blood.* For example, urea is secreted (internal secretion) by the liver, but excreted by the cells of the convoluted tubules of the kidney.

The term egestion is a general one and includes all of those acts which have as their end the *throwing out of excretions especially,* though the term may, not improperly, be used to include not only the throwing out of the excreta, but also of matter which has never formed a part of the body—*e. g.*, the undigested portion of food; and also the unabsorbed part of the inspired air—the nitrogen.

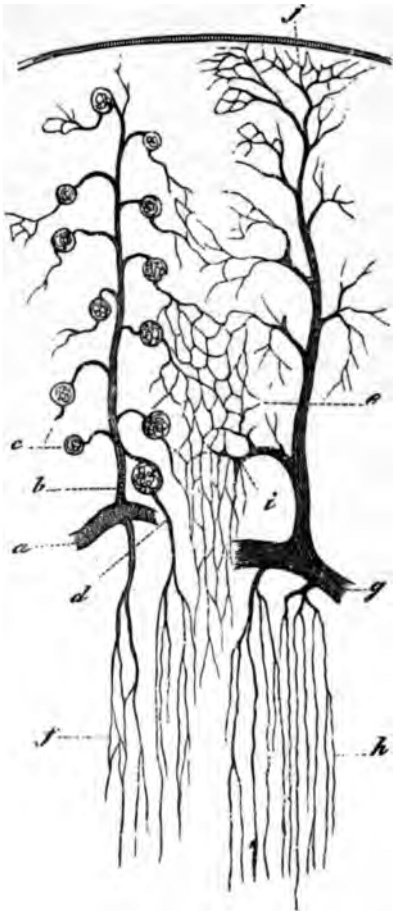
Egestion, then, is represented by the following special acts: (1) Defecation, (2) Micturition, (3) Perspiration, (4) Expiration. The natter thrown out of the organisms by these acts may be called, ollectively, EGESTA; while the term EXCRETA may be used only for *hat part of the egesta* which was at one time a constituent of the ody and has been reduced to a condition useless to the organism nd has been excreted by the lungs, the skin, the kidneys, or the liver.

2. GENERAL CONSIDERATIONS.

We have now followed the process of nutrition to its last stage, –ridding the body of the waste products. We have studied the rocess and products of digestion and have enumerated the factors nvolved in the absorption of digested foods; we have studied xamples of the anabolic changes which occur during the assimilation of the absorbed matter, and of the katabolic changes which ccur incident to the activity of the tissues. We have noted from ime to time the formation of some body useless to the animal organism. 'requently, indeed, these bodies are worse than useless—they may e poisonous. In either case it is necessary that the organism be rovided with some means of throwing off the useless or poisonous natter. But what is the character of this waste matter as we have p to this point noted it? 1st. There was a gas—CO_2—the product f the oxidation of the tissues. 2d. There was water, in part the nchanged water of imbibition, in part the product of oxidation of he hydrogen of the tissues. 3d. There was solid material composed f: (I) certain organic bodies—urea, hippuric acid; (II) inorganic alts—$NaCl$, $HKSO_4$, etc. If one were to compare this list of material '*outgo*" with the list of material "*income*"—the foods—one would ote *a remarkable parallelism in the general character of the matter*— . *e.*, both lists contain a gas, water, and solids composed of organic nd inorganic matter, the organic matter containing nitrogenous and on-nitrogenous bodies and the inorganic matter containing a long ist of chlorides, phosphates, and sulphates. *But the parallelism anishes as soon as one glances at the specific character of the "income" nd "outgo" matter:* the "income" represents matter of high potentiality, while the "outgo" represents matter completely, or almost ompletely, depleted of its energy. The method of liberation and xpenditure of this energy has been discussed.

The only situations where the waste products could be thrown ut of the system are the boundary surfaces. These boundary urfaces include the skin and all of the mucous surfaces, including he genitourinary epithelium. Of all these possible situations ertain locations are specialized for typical secretion only—*e.g.*, enital, conjunctival epithelium; certain locations are specialized or absorption only (villi of small intestines); certain locations re devoted in part to secretion and in part to absorption (epithelium of stomach and large intestine). The only portion of the boundary epithelium which is specialized exclusively for excretion is the *renal epithelium*. The pulmonary epithelium is nearly as much devoted to absorption as to excretion. The general cutaneous surface is, first of all, an organ of protection; secondarily, an organ of thermolysis where the water secreted by the sweat glands serves a specific purpose. Quite subordinate to the two functions mentioned above, the skin is an organ of excretion supplementing the work of the kidneys in the excretion of water.

Fig. 202



Vascular supply of kidney. Diagrammatic. *a*, part of arterial arch; *b*, interlobular artery; *c*, glomerulus; *d*, efferent vessel passing to medulla as false arteria recta; *e*, capillaries of cortex, *f*, capillaries of medulla; *g*, venous arch; *h*, straight veins of medulla; *i*, interlobular vein; *j*, vena stellula. (Cadiat and Schaefer.)

Of the epithelium lining the alimentary canal it cannot be said that it is excretory in any sense. A portion of the secretion (mucus, etc.) passes out of the canal with the feces, but it is secreted for a particular local function and is not separated out of the blood to rid the system of it. The hepatic epithelium, however, forms several excreta, among which are urea, which is excreted by the kidney, and bile pigments, which are excreted by the liver itself.

To summarize: excretion takes place at four more or less specialized parts of the boundary epithelium: (I) *the renal epithelium*, (II) *the pulmonary epithelium*, (III) *the general cutaneous surface*, (IV) *the hepatic epithelium*.

The physiologically important features of the structure of the lungs and of the liver have been summarized under respiration and metabolism. The structure of the skin will be given under the subject External Relations. The only organ solely excretory in its function is the kidney, whose anatomy may be here summarized.

3. ANATOMY OF THE KIDNEY.

ıe following summary presents the facts of greatest importance ıe physiologist:

a. The Blood Supply of the Kidney.

) The large, short *renal artery* direct from the abdominal artery es to the kidney its supply of arterial blood. Its size is wholly

FIG. 203

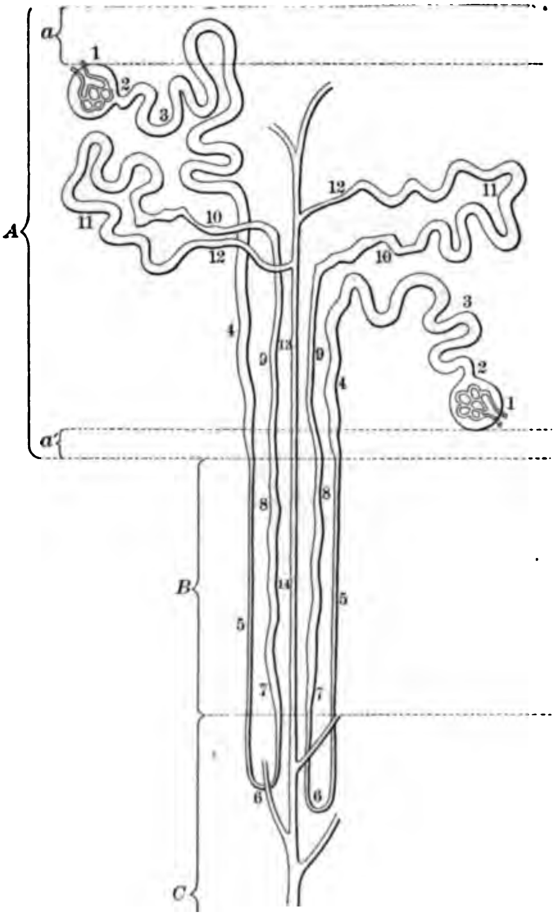


Diagram of the course of two uriniferous tubules. (Klein.)

ɔf proportion to the kidney, making it evident at once that another ɔose than simple nourishment of the kidney tissue is to be accomıed.

(2) The large, short *renal vein* emptying direct into the vena cava offers slight resistance to the return of the blood.

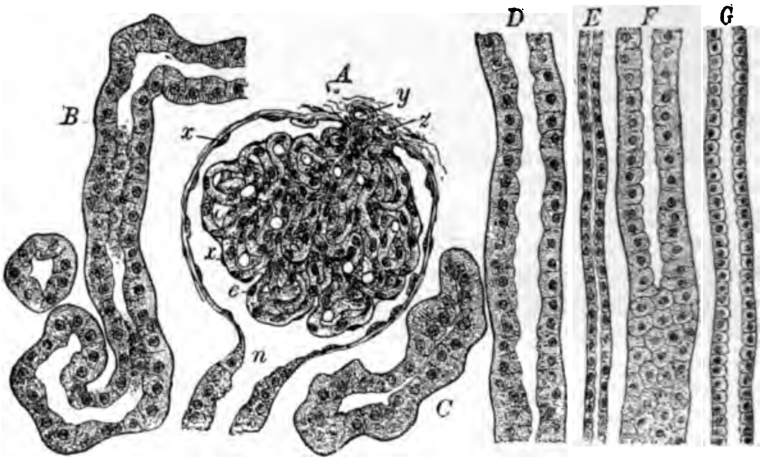
(3) The formation of a network of arterial and venous arches between the cortex and the medulla, in and just below the plane *a*′.

(4) The *interlobular cortical arteries* passing upward from this plane.

(5) The *glomeruli* or tufts of capillaries on either side of the interlobular arteries. Each glomerulus is supplied by an *afferent* arteriole and is emptied by an *efferent* arteriole.

(6) The capillaries of the cortex surrounding in a network the tubules of the cortex and fed by the *efferent* arterioles.

Fig. 204



Portions of the various divisions of the uriniferous tubules drawn from sections of human kidney: *A*, Malpighian body; *x*, squamous epithelium lining the capsule and reflected over the glomerulus; *y*, *z*, afferent and efferent vessels of the tuft; *e*, nuclei of capillaries; *n*, constricted neck marking passage of capsule into convoluted tubule; *B*, proximal convoluted tubule; *C*, irregular tubule; *D* and *F*, spiral tubules; *E*, ascending limb of Henle's loop; *G*, straight collecting tubule. (Piersol.)

(7) The capillaries of the medulla fed by the *true* and *false arteriæ rectæ*.

(8) The *interlobular veins* collecting the blood from the cortex and through the *venous arches*, passing it into the larger branches of the renal vein.

b. The Uriniferous Tubules.

(1) *Capsule* of Bowman enclosing a glomerulus. The glomerulus, though enclosed by the capsule, is outside of the uriniferous canal, because the capsule is reduplicated, one layer of it lying upon the glomerulus.

(2) The *neck* of the capsule, beyond which the real tubule begins.

(3) The *proximal convoluted tubule,* clothed with striated cuboidal pithelium.

(4) The *spiral portion,* with low granulostriated epithelium and avy course.

(5) The *descending limb* of *Henle's loop* possessing the narrowest ımen of the entire tubule, surrounded by flattened plates whose uclei project into the lumen of the tubule.

(6) The *loop of Henle* and the ascending *limb* of *Henle's loop,* with olyhedral cells and flattened nuclei.

(7) The *irregular portion* and the distal convoluted portion, whose pithelium is similar to that of the proximal convoluted portion.

(8) The *collecting tubules* of the *medullary ray,* with cuboidal ansparent epithelium.

(9) The *excretory ducts* of the *medullary portion,* whose epithelium onsists of large, well-defined, columnar cells with ellipsoidal nuclei ear the base.

c. Innervation of the Kidney.

The kidney is supplied by branches from the *renal plexus* which urrounds the renal artery. The renal plexus is, in turn, "formed y filaments from the solar plexus, the outer part of the semilunar lexus, and the aortic plexus. It is also joined by filaments from the planchnic nerves. The nerves from these sources—fifteen or twenty ı number—have numerous ganglia developed upon them. They ccompany branches of the renal artery into the kidney." (Gray.)

The ultimate origin of this plexus is a centre in the floor of the ourth ventricle, anterior to the vagus centre. Section of the nerve ract anywhere between the centre and kidney causes increase in ize of kidney and polyuria or hydruria. Stimulation of the peripheral nd causes shrinking of the kidney and decrease of excretion. These xperiments lead to the conclusion that the renal plexus carries rincipally *vasoconstrictor* fibres. Other experiments show that here are vasodilator fibres. The existence of a specific secretory entre has not been demonstrated.

The discovery of nerve filaments between cells of the convoluted ubule (Berkley), which nerves could hardly have any other function han to influence the secretory activity of the cells to which they are istributed, leads one to the belief that a centre for the control of landular activity of the kidney must exist. The response of the xcised kidney, in size and activity of excretion, to certain perfused rugs would point either to a local secretory centre or to local response f the glandular tissue to the stimulus of the drugs.

THE PHYSIOLOGY OF EXCRETION.

A. RENAL EXCRETION.

1. THE URINE.

a. General Characteristics.

1. **The Quantity.**—An average-sized man passes about 1200 c.c. in twenty-four hours. This amount varies from 800 c.c. to 1600 c.c. according to various conditions, the chief factors which increase the quantity being increased imbibition and decreased perspiration. Either of these two things or both together usually accounts for increased urinary excretion.

2. **The Specific Gravity.**—The urine consists of a number of soluble solids in solution. The amount of the solids is less variable than the amount of the water, but the proportion may vary considerably. The specific gravity varies between the usual normal limits 1015 and 1025. The factors enumerated above which increase the quantity, at the same time decrease the specific gravity because it is the water rather than the solids which is increased. If the limits given above are exceeded in either direction the cause should be determined. To pass beyond these limits does not by any means necessarily indicate a pathologic condition. Halliburton gives as extreme physiologic limits 1002 after excessive imbibition and 1035 after copious sweating. But these are unusual limits, and habits which could lead to such extreme dilution or condensation of urine might readily lead to nutritional disturbances.

3. **The Reaction.**—Normal human urine is usually acid when passed. The urine of carnivora is strongly acid; that of herbivora and vegetarians is either faintly acid or alkaline. The acidity of urine is due to the presence of acid sodium phosphate (NaH_2PO_4). In average urine about 60 per cent. of the phosphoric acid present is in the form of NaH_2PO_4. The generally accepted theory is that when other acids pass into the blood from the metabolic tissues or the absorptive surface they take bases from the monohydrogen phosphate and thus increase the dihydrogen phosphate, so increasing the acidity *indirectly*, the acid body in the urine being in every case *dihydrogen phosphate*, particularly NaH_2PO_4. However, according to the ion theory: *The acid reaciton of a mixture is dependent upon the number of hydrogen ions present.* Therefore, the various acids must take part in the acid reaction in proportion to their dissociation. (Hammarsten.)

Bunge called attention to the fact that the secretion of HCl into the lumen of the stomach is accompanied by a quantitative (internal) secretion of bases into the circulation. This will tend to decrease the acidity of the urine, because the alkali thus liberated combines with the acids produced in other metabolic processes, forming neutral salts and protecting monohydrogen phosphate from the acids in question. This accounts in part for the decreased acidity of the urine during digestion.

It was stated above (Metabolism) that the katabolism of proteins results in the formation of NH_3, which immediately combines to form various ammonium salts. These ammonium salts are excreted mostly in the form of urea. If, however, usual conditions are modified and a larger amount of free mineral acid appears in the blood than can be combined with the Na and K available, then the ammonium takes the place of these alkalies, and the urea excretion is proportionally lessened. Experimentally this can be pushed to the point where urea nearly disappears from the urine. Physiologically this fate of the ammonia is probably very insignificant.

The reason for alkalinity of the urine of herbivora is that their food contains a considerable quantity of alkaline bases (Na and K) in combination with the organic acids (tartaric, citric, malic). These acids become oxidized in the body and the metals combine with CO_2 to make carbonates, whose excretion in the urine neutralizes the acids and leaves the liquid alkaline in reaction.

To SUMMARIZE: *The reaction of the urine is, in man, normally acid. The acidity is due to acid phosphates. The acidity is increased by increased protein metabolism. The acidity is decreased by ingestion of the bases in combination with organic acids. The acidity is decreased by the gastric secretion of HCl. The alkalinity of the blood is decreased (acidity of urine increased) by the secretion of the bile and pancreatic juice.*

4. **The Color.**—The normal light yellow varies with the specific gravity, shading into brown with increasing specific gravity and becoming almost as clear as water with decreasing specific gravity.

b. The Chemical Composition of the Urine.

THE CHIEF URINARY CONSTITUENTS.	PARKES.			BUNGE.	
	Percent. composition.	Quantities in 24 hours.	Per diem per kilo body weight.	Per diem on meat and water diet.	Per diem on bread, butter, & water.
	Grams	Grams	Grams	Grams	Grams
Urine	100.00	1500.0	28.9657	1672 c.c.	1920 c.c.
Water	95.164	1427.46	22.8600		
Solids	4.886	72.54	1.1057	90.607+	45.448+
Organic	3.008	45.04	0.6794	?	?
Nitrogenous	2.336	35.04+	0.5284	70.761+	21.814
Urea	2.212	33.18	0.5000	67.200	20.600
Kreatinin	0.060	0.91	0.0140	2.163	0.961
Uric acid	0.037	0.55	0.0084	1.396	0.253
Hippuric acid	0.027	0.40	0.0060	?	?
Xanthin bodies Amido-acids Aromatic substances Carbohydrates Other organic bodies including pigments	0.666	10.00	0.1510	?	?
Inorganic	1.833	27.50	0.4263	19.846	13.634
Acids	0.845	12.67	0.2045	11.928	7.919
Chlorine	0.500	7.50	0.1260	3.817	4.906
Phosphoric [P_2O_5]	0.211	3.16	0.0480	3.437	1.656
Sulphuric [SO_3]	0.184	2.01	0.0305	4.674	1.265
Bases	0.988	14.88	0.2218	7.918	5.715
Sodium	0.789	11.09	0.1661	3.991	3.923
Potassium	0.167	2.50	0.0420	3.308	1.314
Ammonia	0.051	0.77	0.0130		
Calcium	0.017	0.26	0.0004	0.328	0.339
Magnesium	0.014	0.21	0.0003	0.291	0.139

c. The Urinary Constituents Separately Considered.

The quantity of *water* eliminated from the system by way of the kidneys is far more constant than the quantity ingested, the range of the former being about 500 c.c. (1200 to 1700), while the range of the latter is as much as 1000 c.c. One of the excretory organs must present a range sufficiently wide to cover that shown by the water imbibed. The skin fulfils this requirement. The relation between the quantity of water ingested and that excreted by skin and kidneys, together with the reciprocal relations between skin and kidneys, will be discussed at length with the functions of the skin.

The quantity of *solids* excreted by the kidneys is subject to a considerable range. Note in the above table that with a meat diet the solids are about twice as great in quantity as with a bread diet; and that with a mixed diet (second column) the quantity is midway between that of the pure protein and the vegetarian diet. By far the greater part of the solids leaves the body by the kidneys.

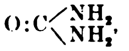
1. **Organic Compounds.**—The relation between organic and inorganic varies within rather wide limits; for a mixed diet the organic : inorganic : : 5 : 3; for a meat diet the organic matter is probably at least four times as great in quantity as the inorganic,

while with the vegetarian diet the relations approach those of a mixed diet.

(*a*) **Nitrogenous Compounds.**—About 94 per cent. (15 grams daily) of the nitrogen leaves the body through the kidneys; the remaining 6 per cent. (1 gram daily) leaves the body in the intestinal secretions, cutaneous and pulmonary. The nitrogenous excreta are much affected by the diet. Note that with a meat diet they aggregate twice as much as with a mixed diet. Of the nitrogen of the urine about 86 per cent. is in the urea, 3 per cent. in kreatinin, 2 per cent. in uric acid and xanthine bodies, 6 per cent. in other nitrogenous compounds, including hippuric acid, amido-acids, indol, skatol, pigments, and nucleoalbumin; and 3 per cent. in ammonia.

Ammonia should probably be classified with the nitrogenous compounds, but inasmuch as it appears as a base among the inorganic constituents of the urine the author has classified it as an inorganic base, under which head it will be discussed.

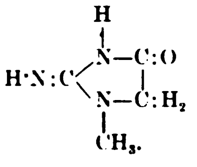
(*α*) UREA OR CARBAMIDE,



$$O{:}C\begin{matrix}\diagup NH_2\\ \diagdown NH_2\end{matrix},$$

is the most important of the nitrogenous compounds. The average amount is about 33 grams per day, though with a meat diet it may be twice as great. No portion of the urea is formed in the kidney. That organ is the excretory organ alone. As already stated above, under metabolism, nearly all of the urea is *formed in the liver;* and, for the most part, probably from ammonium carbonate by double dehydration. The source of the ammonium carbonate from the products of katabolism has been discussed above. (See Metabolism.)

(*β*) KREATININ, or Glycolyl methyl guanidin, or



As has been stated above, the kreatinin of the urine probably comes from the kreatin ingested with lean meat. This ingested kreatin is dehydrated in the liver and excreted directly by the kidneys. (See p. 466.) The fate of the kreatin which is found in the muscles is still a matter of conjecture. The fact that when food is free from kreatin the urine is free from kreatinin would seem to indicate that the sole source of kreatinin is the kreatin of the food. On the other hand, the excretion of kreatinin during starvation seems to decrease the force of the preceding observation. The fact that kreatin is present to the extent of 0.3 per cent. in muscle tissue does not necessarily indicate that it is one of the usual midproducts. It may accumulate to the extent indicated above and remain a fairly constant constituent, little being normally added to the supply and little taken away. If it is being constantly formed it may be completely katabolized to H_2O, CO_2, and NH_3, and the end katabolites built up to the urea level again; or it may be subjected to a series of changes such as that outlined on page 375.

(γ) Uric Acid.—Uric acid is the principal constituent of avian excrement. In the mammalian urine it is an important and constant constituent, though the quantity is small (about 0.5 gm. per diem) compared with that of urea. The fact that when uric acid is given to a mammal, mixed with food, it is hydrated and oxidized to urea and CO_2[1] makes it probable that uric acid is one of the antecedents of urea.

"Through the researches of Horbaczewski,[2] we now know that the nuclear uric acid, as we may term it, is formed together with the xanthin (purin) bases in all organs of the body, and is most abundantly produced in those which are especially rich in nuclei, such as the spleen and the lymph glands. Considerable amounts of uric acid could be obtained from these parts when the blood used in transfusion experiments contained much oxygen, while with the venous blood xanthin bases only were produced. In the amphibia and fish, in which the oxidation processes are especially sluggish, we accordingly find xanthin bases, but little or no uric acid.

"Why is it that in mammals uric acid appears in the urine at all, in view of the fact that uric acid which is introduced into the stomach is eliminated as urea? There is reason to believe that the uric acid thus ingested is carried direct to the liver and oxidizes to urea by the oxidizing ferments of that organ. We find that an increased elimination of uric acid results at once, when the blood of the portal vein is prevented from flowing through the liver by establishing a so-called Eck fistula between this and the inferior vena cava, the hepatic artery being at the same time ligated. In this manner the blood of the spleen and the extensive lymphatic districts of the intestinal tract is carried directly to the general circulation, and the xanthin bases find their way into the urine without being subjected to the action of the oxydases of the liver. We may hence conclude that the appearance of the xanthin bodies in the urine is not under normal conditions owing to the fact that not all of the blood of the body reaches the liver before being carried to the kidneys." (Simon.)

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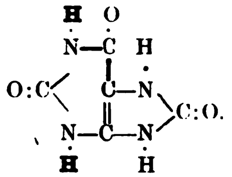
[1] Emil Fischer. Ber. d. deutcher Chem. Gaz., 1884, Bd. xvii.

[2] Summarized by Simon, Physiological Chemistry, p. 258.

Medicus' formula for uric acid is as follows:



Note that the addition of $2H_2O + 3O$ would reduce this molecule to 2 urea + $3CO_2$.

Normal urine contains no free uric acid, but contains several combinations of uric acid with bases: ammonium urate, sodium urate, potassium urate, calcium urate, lithium urate, etc. Their composition is shown by simply displacing one or more of the hydrogen atoms with the metal. The displaceable hydrogen atoms are indicated by heavier type in the formula. Little is known of the relation which these combinations sustain to the metabolism.

Carnin, or Dimethyluric acid, has been found in traces in urine; the two CH_3 radicals displace the two hydrogen atoms indicated above.

Considerable difficulty has been experienced by those who have worked in this field in determining the relations of the metals to the uric acid. To facilitate the explanation of this subject as now understood, we may represent the uric acid formula thus: H_2U; H_2 being the two displaceable hydrogen atoms and U representing the remainder of the uric acid formula: M_2U would represent a *neutral* urate (*e. g.*, Na_2U neutral sodium urate); MHU would represent an acid urate or a *biurate;* $H_2U{\cdot}MHU$ would represent a hyperacid salt or *quadriurate.* Neutral urates are decomposed by H_2CO_3 or by carbonates. They cannot then exist in the blood or in the urine. The acid urates (MHU) are very stable salts; they are less soluble than the neutral salts, but much more soluble than uric acid.

Though urine when excreted contains no free uric acid, this appears usually as a crystalline deposit after the urine has stood, which represents a part of the uric acid freed from the metals. It has been supposed that it was set free by the acid phosphates present in the urine.

$$MHU + MH_2PO_4 = H_2U + M_2HPO_4.$$

Sir William Roberts[1] believes that the above reaction does not represent completely the situation; "*that uric acid is excreted as a quadriurate; that, being in aqueous solution, the quadriurates are in a state of unstable equilibrium and tend at once to decompose according to the equation:*"

$$\text{(I)}\ MHU{\cdot}H_2U = MHU + H_2U.$$

---

[1] Quoted by Hopkins, in Schafer's Text-book, vol. i. p. 589.

The liberated uric acid is precipitated. After this preliminary decomposition the following reaction takes place, in which two molecules of biurate are combined to form one of quadriurate:

$$\text{(II) } 2MHU + MH_2PO_4 = MHU{\cdot}H_2U + M_2HPO_4.$$

This quadriurate may now be decomposed (I) and the resulting biurate combined (II), and so on until all of the urates are decomposed and the uric acid liberated.

Hopkins calls attention to the fact that it is not demonstrated that equation (I) occurs first. The uric acid may be excreted as a biurate and formed by acid phosphate into quadriurate as shown in equation (II). The two equations could alternate just the same according to this proposition and the uric acid be eventually all liberated.

The amount of uric acid is only about 0.5 gram (0.2 to 1) daily on a usual mixed diet. The ratio of uric acid to urea is thus about 1 : 60. Some have emphasized this ratio as having considerable physiologic significance, being a *physiologic constant.* A glance at the table giving the composition of urine shows that diet alone may disturb this ratio—with a meat diet the ratio is 1 : 48, while with a bread diet it is 1 : 82.

Even on the same diet and with the same habits some individuals will excrete much larger amounts of uric acid than others. This individual element must be taken into consideration in clinical cases.

The present state of our knowledge of the relation of uric acid to mammalian metabolism may be thus briefly summarized:

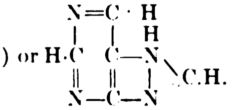
(I) Uric acid and the purin bodies in general result from the katabolism of nucleoproteids. The nucleoproteids thus katabolized arise partly from the disintegration body cells and partly from digested cells taken as food.

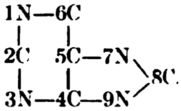
(II) The amount of uric acid (and others of purin series) present in the excreta will vary with the cell (nuclear) destruction. But this in turn varies (I) with destruction of body cells in excessive exercise and in leukocytosis; and (II) with destruction of food cells, the amount in a meat diet being over five times that of a bread and butter diet.

(III) Any interference with normal oxidation in the tissues tends to increase the quantity of purin bodies at the expense of the uric acid.

(*b*) THE PURIN SERIES, INCLUDING THE XANTHIN BODIES.—Uric acid belongs to this series. Emil Fisher discovered purin and classified the members of the series. His classification will be adopted. To purin and its nucleus Fisher gives the following formulas:

Purin ($C_5H_4N_4$) or





Purin nucleus.

'urin itself is not found in the body fluids or tissues because it lizes readily into the other members of the series. Fisher numbers atoms of the nucleus in order to represent by a word formula structure of the various derivatives.

i) *Hypoxanthin*, or *Sarcin*, is a monoxypurin, the oxygen atom ng joined to the 6C atom; it is, therefore, called 6-oxypurin.

ii) *Xanthin* is a dioxypurin. Its structure is indicated by the icture name: 2, 6-dioxypurin, the oxygen atoms being joined to nucleus at positions 2 and 6.

iii) *Uric acid* is a trioxypurin (2, 6, 8-trioxypurin).

iv) *Amino-purins* are represented by *Adenin* (6 amino-purin) and *Guanin* (2-amino-6-oxypurin).

ll of these bodies are normally found in tissues and fluids of the ly and in urine. As stated above, they are products of katabolism he nucleus. The Sarcin, Xanthin, and Uric Acid represent prossive steps in oxidation.

v) *Methyl Dioxypurins* or *Methyl Xanthins* are represented by the lloids theophylline, theobromine, and caffeine, constituents of tea, oa, and coffee, and, therefore, food adjuvants.

a) Theophylline (1, 3-dimethylxanthine) is excreted as: 1-methylthine. (*bb*) Theobromine (3, 7-dimethylxanthine) is excreted in the ie as 7-methylxanthine. (*cc*) Caffeine (1, 3, 7-trimethylxanthine) ears in the urine as 1 to 7-dimethylxanthine. From this it appears the methyl group joined to the 3N is particularly open to oxida- in the body.

he work of Horbaczewski and of Minkowski indicate that the abolism of nuclein takes a course somewhat as follows:

- :lein
  - Nucleic acid
    - Phosphoric acid.
    - Purins . . . .
      - Hypoxanthin + O_2 = Uric acid.
      - Xanthin + O = Uric acid.
      - Adenin + O_2 + H_2O = NH_3 + Uric acid.
      - Guanin + O + H_2O = NH_3 + Uric acid.
  - Protein.

he oxidation is never complete, unoxidized remnants of the ins being found in the urine. The normal daily uric acid excretion bout 0.7 gm., that of the purin bases about 0.1325. The amount he purin bases in the excretion may be quadrupled in leukoiemia (Lusk).

:) HIPPURIC ACID, OR BENZAMIDOACETIC ACID,

$$C_6H_5—CO·NH_2—CH_2—COOH$$

nder metabolism it was stated that in the system hippuric acid ormed by a synthesis of benzoic acid with glycocoll or amidoic acid. We may go a step farther and say that when any of benzoic derivatives which contain only one side chain is ingested usually oxidized to benzoic acid, and this in turn synthesized glycocoll to form hippuric acid. Such benzole derivatives are toluene, $C_6H_5—CH_3$; cinnamic acid, $C_6H_5—CHOH—COOH$; phenylpropionic acid, $C_6H_5—CH_2—CH_2—COOH$. Aromatic bodies of this class are present in epidermal tissues of fruits and vegetables. If one eats apple-skins he will increase the excretion of hippuric acid. Hippuric acid then has a double origin: (I) aromatic bodies in the ingesta; (II) protein katabolism. The fact that hippuric acid does not entirely disappear from the urine during starvation indicates that the aromatic bodies may result from katabolism of proteins.

Hippuric acid may combine with metals to form hippurates, in which form it appears in the urine.

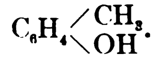
(ζ) AMIDO-ACIDS when ingested are usually katabolized and appear as urea in the urine. But in acute yellow atrophy of the liver and in phosphorus poisoning these bodies pass into the urine unchanged. *Leucin and Tyrosin* are the chief amido-acids so excreted. Cystin, or Dithiodiamidoethidene-lactic acid, is a double molecule. It is an oxidation synthesis of two cystein molecules. Cystein, or Amidothiopropionic acid, is a sulphur-containing katabolite of protein, but it is normally decomposed to simpler products. If not so decomposed it may enter into the following reaction: 2 Cystein + O = Cystin + H_2O. Cystein is quite insoluble in water and appears in urinary sediment in hexagonal plate crystals, or it may form calculi. Certain families present the peculiarity of excreting considerable quantities of cystein (0.5 to 1.0 gram daily).

(η) AROMATIC AND NITROGENOUS AROMATIC COMPOUNDS.—This class of urinary constituents is derived almost wholly from absorbed aromatic bodies. Some of these may exist as such in vegetable tissues; some of them are liberated from or split off from protein during the digestive and decomposition processes which go on in the alimentary canal. Some of these serve an important office in furnishing a vehicle for the removal of the sulphuric acid; the bodies so formed are called Conjugated Sulphates.

There are three subdivisions of this class, viz.: (I) *Hydroxyl aromatic* bodies, (II) *Aromatic oxyacids*, (III) *Conjugated Sulphates*.

(I) *Hydroxyl Aromatic Bodies.*

Phenol, oxybenzole, phenylhydroxide, carbolic acid: $C_6H_5—OH$. (For structural formula see Digestion Introduction.)

Kresol, parakresol,  $C_6H_4\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown OH}$. This body is much more abundant than Phenol.

Pyrocatechin, or orthodihydroxybenzole ($C_6H_4=(OH)_2$), and its isomere *Hydrochinin*, or paradihydroxybenzole ($C_6H_4=(OH)_2$), are both found in human urine; the first only in small quantities, the second only rarely and in traces.

Inosit, or hexahydroxybenzole, $C_6H_{12}O_6$. The quantitative formula of this body is very misleading. One would take it for extrose or, at least, a carbohydrate. It was so considered at first. fter excessive imbibition of water this body, which seems to be ormally present in all the metabolic tissues, will appear in the rine. Its structural formula is indicated in the following:

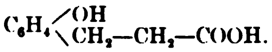
Formula: $C_6H_6 - (OH)_6$.

(II) *Aromatic Oxyacids.* These bodies are derived from Tyrosin -oxyphenylamidopropionic acid) by oxidation and other katabolic anges. The first two are regular constituents of normal urine. he last two are derived from the same source, and are found in rine when intestinal putrefaction takes a certain unusual (perhaps athologic) course.

Parahydroxyphenylacetic acid,

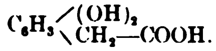
$$C_6H_4\left<\begin{matrix}OH\\CH_2COOH.\end{matrix}\right.$$

Parahydroxyphenylpropionic acid,



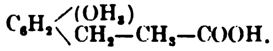
$$C_6H_4\left<\begin{matrix}OH\\CH_2—CH_2—COOH.\end{matrix}\right.$$

Homogentisinic acid, or Dihydroxyphenylacetic acid,



$$C_6H_3\left<\begin{matrix}(OH)_2\\CH_2—COOH.\end{matrix}\right.$$

Uroleucinic acid, or Trihydroxyphenylpropionic acid,



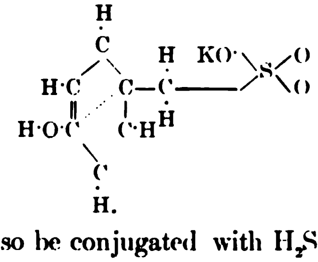
$$C_6H_2\left<\begin{matrix}(OH_3)\\CH_2—CH_3—COOH.\end{matrix}\right.$$

(III) *The Conjugated Sulphates.* Incident to the fermentative rocesses which go on in the alimentary tract, phenol, kresol, indol, nd skatol are formed. These bodies are in part absorbed and pass nto the circulation; their accumulation in the blood would be very eleterious to the system. In the liver they meet the acid sulphate potassium or sodium, or sulphuric acid, and enter into a series of armless combinations which are in due time excreted by the kidneys.

Phenol Sulphate of Potassium has been discussed above. Phenol ay also be conjugated with H_2SO_4 or with $NaHSO_4$.

Parakresol Sulphate of Potassium.

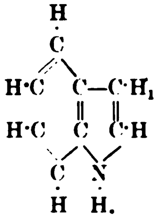
Recall that parakresol = paramethylphenol and the composition this body will be at once understood:

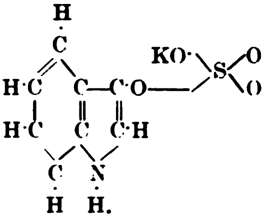


Parakresol may also be conjugated with H_2SO_4 or with $NaHSO_4$.

Indoxyl Sulphate of Potassium, or INDICAN.

Indol is one of the katabolites of intestinal fermentation:

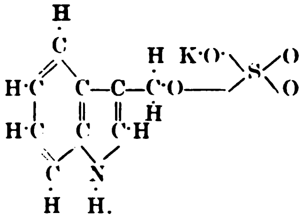




If H_1 be displaced by —OH, indoxyl results. The conjugation of $KHSO_4$ with indoxyl results in the formation of indican with the release of H_2O. Indoxyl may also conjugate with H_2SO_4 or $NaHSO_4$.

Skatoxyl Sulphate of Potassium.

Skatol = Methyl-Indol, the H_1 of indol giving place to CH_3. One of the hydrogen atoms of the methyl may be displaced with KSO_4, to form the body in question.



(*b*) **The Carbohydrates of the Urine.** (I) *Dextrose.*—The urine of the average individual, living an ordinary life, upon an ordinary diet, generally contains sugar—dextrose (Hopkins). This normal sugar is *small in amount.* Excessive ingestion of sugar is likely to be followed by a much increased excretion of sugar—*alimentary glycosuria.* In certain diseased conditions—especially in diabetes mellitus —the excretion of dextrose is excessive, sometimes exceeding 500 grams a day—*pathologic glycosuria.*

(II) *Lactose* is a normal constituent of the urine of women during lactation. It may be found in minute quantities, and during a portion only of the lactation period. When lactation is suddenly checked the excretion of lactose may be considerable.

(III) *Pentoses* (*e. g.*, xylose, arabinose), $C_5H_{10}O_5$, appear in the urine after the ingestion of cherries, plums, etc., where pentoses exist as "fruit-gums."

(IV) *Isomaltose* is said to be present in normal urine.[1]

(V) *Glycuronic Acid*, $COOH—(CHOH)_4—CHO$, is derived from glucose by oxidation of the primary alcohol group CH_2OH to the carboxyl group COOH. It is excreted only in traces in the urine, generally conjugated with some of the aromatic bodies to 1st, Phenolglycuronic acid; 2d, Indoxylglycuronic acid; or, ıtoxyl-glycuronic acid.

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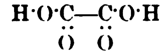
[1] Baisch, Zeitschr. f. physiol. Chem., Bd. xx., S. 249; quoted by Hopkins

ther Organic Compounds.—(*a*) OXALIC ACID $(COOH)_2$, or



$$H{\cdot}O{\cdot}\underset{\overset{\cdot\cdot}{O}}{C}—\underset{\overset{\cdot\cdot}{O}}{C}{\cdot}O{\cdot}H,$$

mal constituent of urine. It is supposed to come from ingested le oxalates, though it does not wholly disappear from the uring flesh diet or during starvation.[1] It readily forms *calcium* which is found in crystalline form in urinary deposits.

HE FATTY ACID SERIES.—Traces of such volatile fatty acids c, formic, propionic, and butyric acids. They are supposed he result of bacterial decomposition in the large intestine. acids once absorbed are less readily oxidized in the system e higher members of the same series.

RINARY PIGMENTS.—As stated above under (4) *color*, the color (light yellow) varies in a general way with the relative of water present, getting darker with increasing specific If the color of the urine were due to the presence of one t only, it would be possible to contrive a scale of colorimetric ıich might be of considerable clinical value. But there are at ur pigments present and the color of each is different, so that nge of the color of the urine depends upon the relative amounts four pigments and is a qualitative change as well as a quanti- ne. Thus far attempts at a colorimetric determination have of no value. The four urinary pigments now known are: *chrome*, (II) *Urobilin*, (III) *Uroërythrin*, (IV) *Hæmatoporphyrin*.

rochrome. This pigment of the urine may be separated by on with alcohol, urine which has already been saturated mmonium sulphate. After the urochrome is removed the s almost colorless. The pigment is easily soluble in water. ıs solutions of pure pigment have the typical urine color. ıs certain that urochrome is the pigment which more than ıer gives the usual color to the urine.

Urobilin, as its name implies, is closely related to the bile ts. It is unquestionably identical with stercobilin, a pigment eces also derived from the bile. It is found in the bile which lergone partial decomposition without access of air. It seems lentical with hydrobilirubin, though this has not been demon- Hydrobilirubin is derived from bilirubin by hydration and on.

$$C_{32}H_{36}N_4O_6 + H_2O + H_2 = C_{32}H_{40}N_4O_7$$
$$\text{Bilirubin} + H_2O + H_2 = \text{Hydrobilirubin, or } \textit{Urobilin}.$$

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[1] Marfori. Quoted by Hopkins. Schafer's Text-book, vol. i. p.614.

(III) *Uroërythrin* is the pigment which colors urinary deposits pink. It exists in normal urine in traces only. Neither physiologic nor pathologic importance has been ascribed to this pigment.

(IV) *Hæmatoporphyrin* ($C_{32}H_{32}N_4O_6$) is present only in traces in normal urine, but may become an important constituent in certain pathologic urines.

(V) *Chromogens* are present in the urine and the use of reagents for general analytic purposes may cause the appearance of some pigment which may be confusing if not understood. *Indoxyl* is a chromogen which easily oxidizes to indigo blue or its isomere indigo red. The following equation represents the reaction:

$$2 \text{ indoxyl} + 2O = 2H_2O + \text{indigo blue} \left(C_6H_4 \left\langle {CO \atop NH} \right\rangle C = \right)_2.$$

Oxidizing agents added to the urine may give rise to either or both of these pigments (indigo blue, indigo red). But the addition of nitric acid readily decolorizes these pigments by further oxidation.

Pathologic urines may contain normal pigments in abnormal quantities or such abnormal urinary pigments as: *hæmoglobin, methæmoglobin, bilirubin, biliverdin, carboluria,* etc.

2. **Inorganic Constituents of the Urine.** (*a*) ACIDS.—(I) *Sulphuric acid and its compounds* are excreted to the extent of 2 to 2.5 grams per diem on a mixed diet and as low as 1¼ grams on a bread diet. (See table of urinary constituents.) The sulphur is ingested as a constituent of the proteins. The excreted sulphur is in part (⅕) combined in such forms as cystin, possibly also sulphocyanides, and biliary taurin (pathologically), but most of it (⅘) is in the form of sulphates. Of these the conjugated sulphates, discussed above under aromatic compounds, comprise 10 per cent., while the inorganic sulphates comprise 90 per cent. The inorganic sulphates are Na_2SO_4, $NaHSO_4$, K_2SO_4, and $KHSO_4$.

(II) *Phosphoric acid and its compounds* are excreted to the extent of about 3 grams daily on an average diet. This quantity is somewhat increased by a meat diet and reduced to about half as much on a bread diet. There are phosphates present in abundance in vegetable foods, but they are mostly in insoluble forms (unabsorbed) forms. There are phosphates of Ca and Mg; but most of the phosphoric acid is combined with Na and K.

To the acid sodium phosphate (NaH_2PO_4) the urine owes its acid reaction. Calcium phosphate may form a characteristic portion of the deposit from feebly acid urine; while the triple phosphates of magnesium and ammonium frequently separate out in crystals which take the forms of "feathery stars" or "coffin-lids." Phosphates are decreased in nephritis and are increased in certain neuroses.

(III) *Hydrochloric acid* is found in a free state only in the gastric secretion. Any part of the HCl which may be absorbed from the limentary canal with the food becomes quickly neutralized through mbination with carbonates of the blood. The major portion of hlorine is absorbed and excreted in the form of NaCl, the integrity f the sodium chloride molecule being usually unimpaired during e metabolic processes. The amount of NaCl in the circulating uid remains fairly constant. An increased ingestion of this salt is llowed by an increased excretion of it. NaCl seems to be retained the system during febrile conditions and to be excreted more eely after the condition becomes normal.

(iv) Other acids: Carbonic acid is present in acid urine and car-onates in alkaline urine. Nitric acid combined as nitrates, which re not products of metabolism, but are ingested with the food.

(β) Bases.—(i) *Sodium* in common salt is used so freely by many s a condiment that its excretion may vary within wide limits; 5 grams er diem is the amount given by Hopkins as an average. Parkes in ne table (urinary constituents) gives more than twice that much. his difference is undoubtedly due to individual differences in the use f salt with the food. This metal is excreted mostly as a chloride, ut also as a sulphate and a phosphate.

(ii) *Potassium* varies very much with the diet, being much more bundant with a meat diet than with a vegetable diet.

(iii) *Calcium* and (iv) *Magnesium* are both present in considerable uantities in the food, but as they are in insoluble forms (phosphates) small amount only is absorbed. These salts are important in bone aking and tooth development, and are, therefore, found in abun-ance in both milk and eggs. Hoppe-Seyler[1] found that the excretion f calcium salts is much more abundant during rest than during xercise.

(v) *Ammonium*, when ingested as ammonium carbonate, is excreted s urea, being dehydrated in the liver. Incident to the katabolism f proteins nascent H and N are liberated and they at once form H_3, which in turn probably joins with CO_2 and H_2O to form mmonium carbonate, which undergoes in the liver the same fate that he ingested salt undergoes. Ammonia may be joined to sarcolactic cid to form ammonium lactate, which in mammals is in turn changed o urea, CO_2, and H_2O, though in birds it is changed to uric acid by he liver.

If HCl be fed to a dog, ammonia, which would under normal onditions appear as urea, is used by the system to neutralize the acid, hus decreasing the NH_4Cl of the urine.

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[1] Zeitsch. f. physiol. Chem., 1891, Bd. xv., S. 161; quoted by Hopkins.

2. THE PROCESS OF URINARY EXCRETION.

a. Glomerular Excretion.

1. **Experiments.**—It has been discovered that the newt has, in common with several other amphibia, a double renal circulation. The glomeruli are supplied by the renal arteries, and the convoluted tubules by the venæ portæ, branches from the femoral vein.

Experiment (I). Inject sugar (or any crystalline and easily diffusible substance into the blood). It will reappear in the urine. Tie the renal arteries and the sugar will cease to be excreted. Conclusion: Sugar is thrown out of the blood by the glomeruli.

Experiment (II). Inject urea into the blood. It will be excreted. Tie the renal arteries and the urea will continue to appear in abnormal amounts.

Experiment (III). Inject a mixture of sugar and urea. Both will be excreted. Tie the renal artery and sugar will cease to be excreted, but the urea will continue to appear in abnormal amounts; thus the result of experiments (I) and (II) are confirmed.

This series of experiments was first performed by Nussbaum. From these experiments, and many others, we may accept it as conclusively demonstrated that the glomeruli excrete the water and easily diffusible salts.

2. **Factors Influencing Glomerular Excretion.** (*α*) IT VARIES WITH LOCAL BLOOD PRESSURE.—But local blood pressure varies as the heart force—terminal resistance remaining the same, or inversely as local terminal resistance—the heart force remaining the same; that is, if the local arterioles dilate through the influence of vasodilator impulses the local pressure in the capillaries of the glomerule will increase and the volume of flow through them will be proportionally increased.

(*β*) IT VARIES WITH THE FULNESS OF THE VASCULAR SYSTEM.—(I) Increased after copious drinking of water; (II) decreased after copious perspiration. Now, this decrease or increase of water occurs without any essential change in blood pressure; therefore, the glomeruli must have an independent action other than filtration.

(*γ*) DIURETICS act by modifying some one of these factors: (I) Digitalis, by increasing heart force. (II) The nitrites, by causing local dilatation of vasæ afferentia, and, therefore, increased by local pressure. (III) Caffeine and many other drugs, however, stimulate the glandular activity of the epithelium of the convoluted tubules, and, therefore, increase the urea, uric acid, etc., of the urine without appreciably varying the volume. Lauder Brunton, of Oxford, urges the great importance of distinguishing two classes of diuretics: 1st, those which stimulate glomerular excretion of water and salts, and, 2d, those which stimulate glandular excretion of the poisonous urea, etc.

(*δ*) VELOCITY AND VOLUME OF CIRCULATION AS ACTIVE FACTORS.—Convenient as it is to believe that the process of glomerular excretion is one of simple filtration—*i. e.*, that it varies as the pressure—we are forced by numerous observations and experiments to believe that some other factor or factors are at work in the process. Any condition which increases the pressure, but at the same time decreases the velocity, will decrease the rate of excretion of water. A partial occlusion of the renal vein has the effect of increasing pressure and decreasing velocity. A complete occlusion of that vein stops water excretion and injures the organ, so that a removal of the occluding ligature is followed by a copious excretion of albuminous urine. It is supposed that the high pressure in the glomerulus mechanically stops filtration by pressing the glomerular epithelium against the walls of the Bowman capsule; further, that this pressure and tension on the glomerular epithelium injures it so that it is no longer able to perform a selective activity, and lets serum albumin filter through. On the whole, it is concluded[1] that it is an increase in velocity and volume of circulation rather than simple increase in pressure which is the *essential factor.*

b. Glandular Excretion or Excretion by the Epithelium of the Convoluted Tubule.

Experiments of Nussbaum produce practically conclusive evidence that the epithelium of the convoluted tubule is the seat of the excretion of urea and allied bodies. Von Wittich observed that in birds, whose urine contains little water, urates may be detected microchemically in the epithelium of the tubules, but not in the glomeruli. If the kidneys be extirpated the urea and allied bodies accumulate in the blood; therefore, these bodies are not formed by the glandular cells of the convoluted tubules; these cells only "separate them out of the blood" and excrete them. We cannot properly speak of the secretion of the urine of the kidneys, but rather the excretion.

c. The Influence of the Nervous System upon Urinary Excretion.

The influence of the nervous system upon the activity of the kidney in excretion can be explained by assuming that the fibres of the renal plexus (see introduction to Excretion) are vasomotor and not secretory. However, the detection of nerve endings among the active cells which line convoluted tubules[2] leads one to believe that their action is influenced, perhaps wholly controlled, by the nervous system.

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[1] Hermann's Handbuch der Physiologie, Bd. v., S. 338.

[2] Berkley, Johns Hopkins Hospital Bulletin, vol. iv., No. 28, p. 1.

The kidney is influenced on the one hand by local blood pressure, and on the other by the constituents of the blood. *In the case of the active cells of the kidney, as in the case of the intestinal cells, we must ascribe a selective function.* Dextrose and urea circulate side by side. The cells of the kidney let urea pass. They do not normally let any appreciable amount of dextrose pass.

d. Summary.

(I) Water and mineral salts are excreted through the glomerular epithelium.

(II) Nitrogenous excreta are separated from the blood by the epithelium of the convoluted tubules.

(III) Glomerular excretion is varied in quantity with the velocity and volume of the circulation of blood through the glomerular capillaries; the velocity of the circulation depends in turn upon the cardiac activity and the local dilatation of arterioles.

(IV) The rate of excretion by the epithelium of the convoluted tubules is free from influence by moderate changes in blood pressure. Certain drugs, such as caffeine, stimulate the glandular activity of the convoluted tubules and thus increase the elimination of urea, uric acid, and related bodies.

(V) The nervous system influences the action of the kidney (i) through vasomotor fibres to the vessels of the kidney; (ii) through general cardiac innervation; (iii) through secretory fibres reaching the active epithelium of the convoluted tubules through the sympathetic system.

e. The Egestion of Urine—Micturition.

The urine passes from the pelvis of the kidney through the ureters to the bladder, where it is retained until that viscus is sufficiently full to stimulate its sensory nerves and so appeal to the consciousness of the individual. The act of micturition consists in voiding the urine in response to this "appeal of nature." The act is partly voluntary and partly involuntary. The initiatory act is voluntary and consists in relaxation of the sphincter, whose tonic contraction retains the urine between the egestive acts. Once the sphincter is relaxed the contraction of the involuntary muscular coats of the bladder is sufficient to empty the viscus, though this force may be supplemented by contraction of the abdominal walls. The final act is the voluntary contraction of the *accelerator urinæ* muscle.

The innervation of the bladder is from two sources: (i) From the lower dorsal and upper lumbar *via* the mesenteric ganglion and the hypogastric nerves. Stimulation of these causes contraction of the circular fibres of the bladder and the sphincter. (ii) From the second and third sacral *via* the nervi erigentes. Stimulation of these causes relaxation of the sphincter and contraction of the detrusor urinæ.

B. PULMONARY EXCRETION.

Of the products of excretion practically all of the CO_2, about one-sixth of the water, and minute quantities of certain organic materials are excreted by the lungs, and leave the body as exhalations from the respiratory organs. For the details of this subject see RESPIRATION.

C. CUTANEOUS EXCRETION.

Excretion is only an incidental function of the skin and is secondary to *protection*, to *general sensation*, and to *thermolysis*. That this is true is evident from the fact that the sebaceous glands secrete fatty products whose function is to keep the skin pliable and non-absorbent, while the other glands—the sweat glands—produce a fluid which is almost wholly water and whose primary function is the regulation of heat by facilitating heat radiation (thermolysis). The reciprocal relation between the amount of water which leaves the body by the kidneys and that which leaves the body by the sweat glands is an evidence that the skin must not be ignored as an organ of excretion.

1. THE SWEAT.

a. General Characters.

1. **Quantity.**—The amount of sweat formed in a day varies between very wide limits; the minimum being about 500 grams and the maximum being about 2000 grams for twenty-four hours, though it may reach a rate of 4000 grams per diem for an hour or more in an experiment. To collect the excretion for experimental purposes the subject's arm or leg may be enclosed in a rubber bag; or the subject may be placed naked in a ventilated chamber, as in the experiments of Voit and Pettenkoffer. In such an experiment Schierbeck[1] found with progressively increasing temperature a progressively increasing excretion of water and of CO_2.

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[1] Arch. f. Physiol., Leipzig, 1893, S. 116; quoted by Reid in Schafer's Text-book, vol. i. p. 671.

EXCRETION OF H_2O AND CO_2 BY SKIN AT VARIOUS TEMPERATURES OF SURROUNDING AIR.

Temperature of Chamber.	H_2O Excretion. Grammes per hour)	H_2O Excretion. (Grammes per 24 hours.	CO_2 Excretion. (Grammes per hour.)	CO_2 Excretion. (Grammes per 24 hours.)
29.8°C.	22.2	532.8	0.37	8.9
30.4° "	27.8	667.2	0.40	9.6
31.5° "	71.9	1725.6	0.37	8.9
32.8° "	73.4	1761.6	0.35	8.4
33.8° "	82.6	1982.4	0.87	20.9
35.4° "	106.8	2563.2	1.04	25.0
38.4° "	158.8	3811.2	1.23	29.5

2. **The Specific Gravity** of human sweat is from 1003 to 1006; the greater the quantity the lower the specific gravity.

3. **The Reaction** of sweat is acid, though when the excretion is copious it may become neutral or even alkaline in reaction. The acidity is due to NaH_2PO_4. On standing the reaction changes from acid to alkaline, due in part to the change of urea to ammonium carbonate.

b. Chemical Composition of Sweat.[1]

Sweat		100.00	
Water		98.88	
Solids		1.12	
1. Organic		0.66	
	(a) Fats and fatty acids		0.41
	(b) Epithelium		0.17
	(c) Urea and other nitrogenous compounds		0.08
2. Inorganic		0.46	
	(a) Sodium chloride		0.28
	(b) Other salts		0.18

1. **The Organic Constituents of Sweat.**—These are in excess of the inorganic, but not so much in excess as in the case with urine.

(α) THE FATS AND FATTY ACIDS are largely derived from the secretion of the sebaceous glands, but when the sweat is collected from the palm of the hand it still contains a small amount of fats and volatile fatty acids. The reaction of the sweat is in part due to the presence of fatty acids. The volatile fatty acids present are: formic, acetic, propionic, butyric, caproic.

(β) THE EPITHELIUM is carried away mechanically. The epithelial scales are composed chiefly of *keratin*, of which sulphur is an important constituent. This is one of the ways in which the sulphur leaves the body.

(γ) UREA AND OTHER NITROGENOUS COMPOUNDS have been demonstrated by Argutinsky[2] to be present in the sweat; in one case finding 0.363 grams of urea in 226 c.c. sweat collected in half an hour. According to Reid the nitrogen excreted by the skin may

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[1] From Charles' Physiol. Chemistry, p. 349; quoted by Halliburton, Text-book of Chem. Physiology, p. 820.

[2] Archiv f. d. ges. Physiol., 1890, Bd. xvi. S. 594.

ial 4.7 per cent. of that by the urine. This amount is greatly
reased in uræmic conditions. Uric acid, kreatinin, etc., have also
en found.

2. **The Inorganic Constituents of Sweat.**—These are made up
efly of *sodium chloride*. *Among other salts* are: potassium chloride,
d sodium phosphate, sodium and potassium sulphates, calcium
d magnesium phosphates. The salts are thus qualitatively equiv-
nt to those of the urine.

THE PROCESS OF CUTANEOUS EXCRETION—PERSPIRATION.

1. **The Influence of the Nervous System upon Cutaneous Excre-
n.**—The sweat glands are provided with (*a*) *secretory* and (*b*) *vaso-
tor* nerves; the latter are represented by both *constrictor* and
ator fibres. The secretory fibres radiate from a centre (or probably
eral centres), in the central nervous system—cord and medulla.
ie centres are stimulated directly (i) by a highly venous condition
the blood; (ii) by a high temperature of the blood; (iii) from the
ebrum; (iv) by poisons: pilocarpine, strychnine, nicotine, etc. The
itres are stimulated reflexly by subjecting the skin to a high
nperature.

2. **Factors which Cause a Variation in the Quantity of Perspi-
tion.**—The total perspiration—500 grams to 2 kilograms daily
either evaporates as it is formed—*insensible perspiration*, or it
lects upon the surface of the skin—*sensible perspiration*.

The total amount of perspiration varies (i) with the temperature
the air, (ii) with the proportion of water in the blood, (iii) with
od pressure, (iv) with the velocity of the blood flow, arising
ually from muscular activity, (v) with the activity of kidneys
d bowels, (vi) with the state of the emotions, (vii) with general
temic conditions—certain diseases are accompanied by profuse
phoresis, (viii) with individual peculiarity, and (ix) with drugs
locarpine). In 'variables (i) to (v) an increase of the variable
uses an increase of the perspiration. In (vi) anything which
uses the skin to flush is likely to be accompanied by perspiration,
ough there is a "cold sweat" also which may accompany fear.

The amount of *sensible perspiration* will depend primarily upon
of the factors which cause a variation in the total amount of
rspiration, and secondarily upon the condition of the atmosphere,
ing increased by higher temperature and decreased by increasing
capacity of air for moisture.

D. INTESTINAL EXCRETION.

Of the various fluids and solids poured into the alimentary canal by the surrounding or tributary glandular epithelium, by far the greater part is to be considered to be typically *secretion*, for it is introduced into the lumen of the canal to serve a particular purpose; after serving that purpose it may be reabsorbed or passed out with the egesta. There are, however, certain substances which must be recognized as excretions: (*a*) *The Bile Pigments:* (I) Bilirubin; (II) Biliverdin; (III) Hydrobilirubin (Stercobilin); (*b*) *The Fat-like Constituents of the Bile:* (I) Cholesterin ($C_{26}H_{43}OH$); (II) Lecithin:

$$C_3H_5 = (C_nH_{2n-1}O_2)_2 - O{\cdot}PO{\cdot}OH - O{\cdot}C_2H_4{\cdot}N(CH_3)_3OH.$$

Lecithin and cholesterin are constituents of nerve tissue. They must be looked upon as nerve katabolites and the liver the organ for the excretion of those katabolites which are peculiar to nerve tissue. (*c*) *Salts.* Certain salts, calcium salts especially, of the bile and of other intestinal liquids must be looked upon as on the way out of the system.

PATHOLOGIC PHYSIOLOGY OF EXCRETION.

1. **Cellular Excretion.**—All cells in the organism have the power to rid themselves of particles that have become useless. They do this by means of cilia, by amœboid movements, by a process of exosmosis.

2. **Tissue Excretions.**—By this we understand the transporting of effete particles to the specific organs of elimination—*i. e.*, the spleen, liver, etc. This conveying, scavenging function is the duty of the lymphocytes (small and large), of the wandering and of the eosinophilic leukocytes. The whole process bears the name of phagocytosis given to it by the illustrious Metschnikoff. Indeed, we look upon internal tissue excretory function as one of the essential factors in the maintenance of the vital functions. This remarkable, almost deliberative sensitiveness of the phagocytic cells constitutes one of the main defences of the human economy. These cells are the sanitary policemen of the body. (I) They carry pigment from any source soever to the liver. (II) They attack, destroy, and then bring the microbes to the places of final extrusion. (III) They load up the heavy metals (Hg, As, Cu, Ag, Fe.) and transport them to the liver, where they are eliminated. (IV) They seize upon the toxin-bearing particles of protoplasm and render them innocuous by their internal secretion and by discharging them into the liver, spleen, glands, etc.

3. **Organic Excretion.**—To this function a number of organs are detailed, each of which has its particular share of the task, while at the same time they supplement each other and take on additional or compensatory work as occasion requires. The specific organs of excretion are the following: the liver, the kidneys, the glands of the skin, and the epithelium of the alimentary tract, especially that of the lower portion.

A. RENAL EXCRETION.

n. S.

The kidneys are the great excretory avenues of the body. The ultimate phases of the circulation of elements take place here. It is in the kidney where osmosis and selective epithelium co-operate in ridding the system of a variety of substances which, if retained, would injure the vital functions. Pathologic physiology considers the manifold factors that may harmfully react upon renal activity, and discusses the ways in which such conditions may influence general health.

The clinical recognition of renal disorders rests mainly upon the changes in the urinary ingredients. Among them the excessive quantity of albumin in its several forms has been thought to furnish the keynote to the pathology of renal disease. Then the presence of various forms of casts was held as a true index of nephritis. Lately the chlorides have received a great deal of attention as being the exponents of glomerular activity. Combined, these three groups of urinary findings (albumin, casts, and alteration in the chlorine output) will enable us to establish the diagnosis of nephritis. This, however, is possible only when the disease is well established. We are as yet not able to recognize the morbid alterations of the kidneys until they have done a great deal of harm to the system. And yet, long before we can gather enough evidence to convince a body of scientific physicians of the real existence of nephritis in a given person, there are a number of foreshadowing, initial, or at least strongly suspicious symptoms which will assist us to detect the presence and, sometimes, the nature of inadequate renal function; that is, of renal insufficiency.

1. RENAL INSUFFICIENCY.

n S

By this is meant deficient urinary depuration. It may be called the early stage of actual nephritis, the prodromal condition of Bright's disease, or even of uræmia. During this condition of inadequacy the various renal alterations are in the process of developing, and the organs lag more and more in their physiologic duties.

1. **Pathogenesis.**—Generally speaking, any condition or factor that will damage one or more of the agencies of urinary secretions

—that is, (I) the character of the blood, especially its rate of flow; (II) the epithelium of the glomeruli, or of the tubules; (III) the vasomotor nerves controlling the adaptation of renal circulation—will, of course, be followed sooner or later by inadequate kidney function. Toxins of internal or of external origin, gaining access to the circulation in some way or other, are the main cause. These poisons slowly added during a long period to the blood invariably produce harmful effects, although in various ways. Firstly, producing through the vasomotor centres increased blood pressure, injuring thereby the intima of the arteries and constituting the real cause of arteriosclerosis. Secondly, upon the renal epithelium directly, impairing its selective activity, which will be followed by the appearance in the urine of albumin, very often of casts, and different ill-known extractives.

2. **Pathologic Physiology.**—(I) Symptoms on the part of the cardiovascular system, arteriosclerosis, hypertrophy of the heart, increased arterial pressure.

(II) The symptom-complex is *small Brightism* (of Dieulafoy), cramps in the calves, paræsthesias—*e. g.*, cold or "dead" finger, sparks in the front of the eyes, dizziness on rapid variation of posture, etc.

(III) *The urinary manifestations of renal insufficiency:* polyuria, pollakiuria; the coloring matter or urine diminished; specific gravity is lowered; there is diminished permeability of the kidneys to methylene blue; and, lastly, cyclic or orthostatic albuminuria. (See latter.)

(III) *The general symptoms* will depend for their existence and character upon the presence or absence of other morbid conditions—*e. g.*, myocarditis, infectious disease, etc.

2. ALBUMINURIA.

There is normally a small amount of albumin in the urine, recognizable, however, only by special and elaborate testing, so that for the clinician there is really no albumin outside of the pathologic correction. The importance of albumin in the urine must under no condition be exaggerated, because (I) its existence does not furnish an index to the severity or even to the exact nature of a given kidney lesion; (II) the causes leading to it are complex, multiply, and very often act simultaneously; (III) albuminuria by itself is not of so deleterious a nature as the harmful substances occurring incidental to its appearance.

Broadly speaking, albuminuria may accompany or follow any condition involving the glomerular or the tubular epithelium which interferes with the renal circulation. Its source is nearly always the albumins of the blood—serumalbumin and serumglobulin—although in many cases it originates from the cellular and nuclear protoplasm of the secreting cells—*i. e.*, nucleoalbumin. Hereditary disposition, circulatory lesions, toxæmias, and toxic infections are the most potent causative factors of albuminuria as well as of nephritis in general. A deliberate yet rapid survey of the experimental and clinical facts known as two main groups of albuminurias is as follows:

a. Functional Albuminuria.

In these cases we are as yet unable to recognize, by means at our disposition, lesions accounting for this phenomenon. For some reason, escaping our detection as well as our speculative sagacity, the kidney fails to retain the albumin of the blood.

(I) Albuminuria in persons *apparently* in *good health.* It is irregular and intermittent.

(II) Albuminuria of *adolescence;* in general, cyclic and intermittent.

(III) Albuminuria, of *digestive* and *hepatic origin.*

(IV) Orthostatic albuminuria (Linossier) occurring in *neuropathic,* hereditarily predisposed persons.

These four varieties of albuminuria have been called physiologic albuminuria (Leube), cyclic albuminuria (Heubner, Senator), and orthostatic albuminuria (Linossier-Lemoine). The complex terminology indicates its main characters as well as its difficult interpretation. There seems, however, enough evidence to justify the following conclusions: Any disturbance of the tenaciously constant albumin, equilibrium of the blood is pathologic, whether we find clinical or post-mortem lesion sufficient to account for it or not. Moreover, an individual may exhibit for a long period a morbid alteration of some function or other without being conscious of it; that is, without ever feeling enough of the disturbance to give rise to subjective complaints.

b. Organic or Renal Albuminuria.

The morbid alterations reside mainly in the kidneys, are due to a selective noxious action of endogenous or exogenous poisons, together with a hereditary instability of the renal secreting and excreting structures.

(I) *Acute* or *infectious* (toxic infectious) nephritis or irritative nephritis. The cause or causes are here followed immediately by correspondingly severe symptoms.

(II) *Chronic* or permanent nephritis. The albuminuria in these cases varies with the state of the renal circulation, with the predominance of glomerular or epithelial lesions.

Symptoms of Albuminuria.—They depend upon the nature of the cause or causes inciting the lesions and upon the coexistence of other morbid lesions (see under head of Urinary Poisoning)—*e. g.*, cardiac or hepatic lesions.

3. EXCRETION OF WATER AND SALTS.

It is now well established that we must distinguish two processes in urinary activity: (I) glomerular function—*i. e.*, selective filtration of water and salts, especially of chlorides; (II) epithelial selective function, partial reabsorption of the glomerular secretion, and excretion of urea, uric acid, and other extractives by the epithelium of the renal tubules.

We have stated above what factors influence the water output through the kidneys, and we so state conclusively that whatever increases the watery constituent of urine also increases the percentage of chlorides. Both of these substances are used to maintain the osmotic equilibrium of the blood and tissues; moreover, there seems to be a specific function of the chlorides, namely, the prevention of accumulation of toxic substances. In other words, they subserve detoxication. The brilliant investigation of Toulouse, Richet, Achard, H. Strauss, Widal, Cushney, *et al.*, have demonstrated that wherever a toxic substance threatens the security of the economy the chlorides are dispatched thither to increase the molecular tensions of the region thus affected. Consequently we witness a diminished urinary output of chlorides in such conditions as fibrinous pneumonia, œdema of cardiac or renal origin, and in certain latent eclamptic and uræmic conditions. Decrease of chlorides in the food causes the retained chlorides of the tissues to release their hold upon them and to be eliminated themselves in conjunction with the noxious substances over which they did guard duty. The glomerular epithelium is endowed with exquisite sensitiveness and reacts promptly to all conditions endangering or favoring the system. By the artificial variation of the osmotic quality of the blood plasma—*e. g.*, by withholding the chlorides from the food or by increased ingestion of water—we can add very materially to the elimination of toxic material from the economy. A hydruria means also a chloruria, and the two together constitute the means of combating retained or newly produced injurious substances.

From the foregoing it is evident that the chlorides preside over the chemical regulation of the tissue fluids. They act rapidly and efficaciously because of their abundance and great diffusibility. Retention of chlorides, as seen by urinary fluid findings, is a witness of the morbid processes going on in the body, although no exact measure of their nature.

4. ECLAMPSIA.

This is a peculiar, and very frequently fatal, intoxication of the system, akin but not similar to uræmia, and occurs in women either pregnant or in the puerperium. Owing to the frequent abnormal urinary findings clinicians and pathologists have attached it since the dawn of medicine to lesions of the renal apparatus. Theories in regard to its pathogenesis have sprouted from the prolific heart and brain of even earnest workers. They bloomed and in due time faded. Thus the theory of decidua-cell migratism (Schmorl).

The mechanical theory of ureteral compression with anuria (Halbertsma) and others have joined the retired list of hypotheses. In fact we are ignorant as to the real causes of eclampsia. It occurs mostly in young and old primiparæ, but we are as yet at a loss to recognize even predisposing causes. The most reasonable views are, perhaps, these: (I) The fœtus inhabits its mother, and has a metabolism of its own which may react injuriously upon that of the mother. This reaction is not unlike that of an autointoxication: failure to adapt itself to the additions poured into the maternal organism by a perverted fœtal metabolism produces an eclampsia. Whether or not this is expressed clinically and observed or not does not alter the case, for only a portion of eclamptic mothers are treated for it. (II) The neuropathic element is of great importance in all cases of eclampsia. Certain women are predisposed to it by reason of their psychic and somatic hereditary instability. A sword of Damocles is suspended over their head, usually without their being aware or conscious of it, and, unfortunately, also out of reach of the physician. We must confess that there is no known curative treatment for eclampsia.

5. URINARY POISONING.

This is a generic term which signifies the intoxications of the system from substances either generated in the body, but improperly eliminated, or poisonous materials produced *de novo* from invading microbes, or from perverted metabolism in other organs. Consequently we can separate urinary poisoning into three main varieties (Guyon): uræmia, urotoxæmia, and urosepsis.

a. Uræmia.

Uræmia is to renal disturbances what acetonæmia is to hepatic maladies. It means the circulation in the blood of urinary excretory substances. Vague as it is, it is clearer and less hypothetic than other terms invented to supplant it. It is an aseptic intoxication from acute or chronic retention of urinary poisons *before their passage through the kidneys.*

In the uræmic syndrome intoxication is only one factor, and it is probable that the perversion of some other internal, possibly renal, secretion plays the main role. For the development of the classic picture of uræmia we must presuppose a certain nervous disposition acquired or hereditary. The greatest obstacles to early recognition are: (I) It may begin very insidiously, and may last a long time without giving rise to any symptom. (II) It may be masked or covered up by symptoms of disturbed digestive, hepatic, or metabolic functions. (III) We do not know exactly upon what external influences the system does react with urinary poisoning. Be all this as it may, uræmia is always a grave, frequently fatal, complication of renal insufficiency, and the causes underlying its origin and character are as yet too intricate to admit of our unravelling them.

1. **Pathogenesis.**—(I) *Intoxication* of the system by urinary poisons and malelimination of the potassium salts and urotoxins are the principal ones. (Bouchard.)

(II) *Excessive* molecular concentration of body fluids. (Korangi, Hamburger.)

(III) *The mechanical theory* of Traube: cerebral œdema resulting in the production of eclamptic seizures due to anæmia of the brain (Zangemeister and Naunyn also believe in this theory). Bouchard's theory satisfies most of all, although we have not as yet succeeded in isolating the real toxic urinary substance. At any rate, it is Bouchard to whom we owe the fundamental experiments upon the coefficient of toxicity of the urinary constituents.

2. **Pathologic Physiology.**—The symptoms of uræmia lean, on the one hand, upon renal insufficiency, and on the other hand upon those of urinary poisoning.

They depend upon a variety of conditions: (I) Presence or absence of infectious or other intoxications—*e. g.*, alcoholism, morphinism, plumbism, pneumonia, septicæmia, etc. (II) Upon the previous state of health of the individual. (III) Upon the manner of onset and the rapidity with which the system is being invaded by the toxins. (IV) Upon the condition of the nervous system of the affected person. (V) Upon the manner of treatment.

However, the morbid signs of uræmia may be caused with usually all or most of the following:

(α) NERVOUS AND PSYCHIC DISTURBANCES.—Hemiplegia, exaggerated reflexes, neuritis, anopsia, amblyopia, retinitis, delusions, mania, depression, aphasia, coma, Cheyne-Stokes respiration, epileptic seizures, etc.

(β) CARDIOVASCULAR SYMPTOMS.—Arterial hypertension, hypertrophy of the left heart, recurrent attacks of dizziness, Stokes-Adams disease, decreased coagulability of the blood.

(γ) GASTROINTESTINAL SYMPTOMS.—Emesis (from excretion into the stomach of toxic substances—Rostoski), diarrhœa, anorexia, etc.

(δ) URINARY FINDINGS.—Albuminuria and casts occur often; they are not infrequently absent. Diminution of chlorides, as a rule;

mpermeability to methylene blue; lowering of the water output of he urine, sometimes even complete anuria; appearance of acetone nd of fatty acids.

b. Urotoxæmia.

We understand by this term that variety of aseptic urinary poisonng which occurs from the resorption of toxic substances after their assage through the kidneys.

Pathogenesis.—It is well known that normal and abnormal urinary roducts can be reabsorbed from any portion of the renal urinary ract beyond the secreting tubules: pelvis, uterus, bladder, deep rethra especially. This form of intoxication occurs mostly after urgical or other trauma to the lower urogenital tract: catheterization, perative interference upon bladder or prostate, etc. Although it ccurs in predisposed individuals, urotoxæmic or urinary sapræmia s attached more closely to its causes than the other two varieties; t begins with them, and, if existing alone, usually ends soon after he cessation of its cause or causes.

c. Urosepsis.

Urosepsis is infection of the urinary tract in any of its portions. It is a toxic infection very frequently accompanied by toxæmia or ræmia. A special hereditary predisposition is not necessary here. The pathogenic microbes gain access to the urinary channels and reservoirs from within or from without. They elaborate a toxin which if resorbed produces the more or less complete picture of epticæmia or of septicopyæmia.

1. **Pathogenesis.**—The *modus operandi* of the causative factors is asy of explanation—*i. e.*, invasion by pathogenic organisms; production and absorption of toxins. Whether or not association of microbes play a decisive role here cannot as yet be definitely stated. There are a number of predisposing factors influencing the onset, nature and course of urosepsis. Thus (I) any obstacle to the flow of urine in any part of the urinary tract invites and facilitates the growth of bacteria—*e. g.*, stricture, stone, enlarged prostate, uretero-hydronephrosis from any cause. (II) Morbid, particularly, suppurative processes in the organs or tissues adjacent to the urinary tract—*e. g.*, prostatitis, appendicitis, metritis, perineal abscess, orchitis, etc. (III) Secondary infection of urinary organs from a primary focus in any part of the system—*e. g.*, osteomyelitis, mixed infection from uppurative foci, etc.

2. **Pathologic Physiology of Urosepsis.**—The symptoms of urinary septic or infectious intoxications are the same as those occurring from infectious suppurating processes anywhere else in the body. But they are, as a rule, associated with uræmic or urotoxæmic symptoms. Consequently the symptom-complex of urinary sepsis is a

protean one and does not admit of close analyzing, because morbid causes aid each other as well as do physiologic functions.

d. Œdema.

Œdema implies the presence of a watery, lymph-like substance in the tissues or cavities of the body. It has always been considered in connection with pathologic alterations of excretion. Theories regarding the genesis of œdema are constantly being constructed, and to-day the same problems agitate the minds of scientific physicians as fifty years ago. The osmotic and the molecular concentration theories have gained in weight in recent years. But animal experiments have not yielded the results expected, and clinicians, as in former years, are the ones to furnish us the most facts. The mechanical theory of Ludwig and the filtration theory of Heidenhain contain each one part of the truth, and to-day we know a third factor—the vital activity of the endothelia of lymph- and blood-vessels.

If we consider deliberately the fact that œdema does occur, often, and from various causes, but always at times when the security of the organism is threatened, we cannot help asking the question why does it occur? Again, when we bear in mind that œdema occurs not only at special occasions, but also in special places, we ask ourselves in all sincerity: Why does œdema occur here and not at some other place?

The thinking student will remember that there is nothing purposeless in nature. The fact that œdema occurs under certain conditions must also have some significance. He may thus arrive at the conclusion that œdema is one of the protective defensive measures of the body against toxic influences, and what he may have been fighting with all his ingenuity has turned out to be his ally. The disturbances of excretion underlying œdema are usually present a long time before the actual transudation occurred. Why, now, does œdema occur at certain places, and what determines its localization?

It occurs at places most in need of protection; that is, where absorption of noxious substances is likely to occur if this hygienic measure is not taken. The nervous system plays a very important role in the localization of œdema. The segmental or metameric distribution advanced by Brissaud certainly betokens the active part taken by the nervous system in dispatching œdematous fluids to a certain region. (Merklen, Widal.)

1. **Pathogenesis.**—There are a number of causative factors in the production of œdema which may act singly or conjointly, as a rule the latter. Earnest enquiries into the purpose of the existence, localization, etc., of œdema shows it to us as a means of defence, and it is *a priori* evident that the pathogenic factors must co-operate

in order to produce this phenomenon. These factors are the following:

(I) Alterations in the osmotic pressure, or water-absorbing power of the tissues, from retention of crystalloids (*e. g.*, NaCl?), formation of acids, etc.

(II) Decrease of the collateral pressure of the tissues surrounding the nutrient vessels (Cohnheim), which may or may not be accompanied by increased intracapillary pressure. This accounts for the early occurrence and recognition of œdema in ill-nourished and dependent parts of the body (ankles, legs, eyelids). This would, in a measure, also include the occurrence of pulmonary œdema as explained by Welch, whose views are, however, not accepted by Senator, Merklen and Chauffard.

It is, nevertheless, a fact that œdema is very rare in the healthy, tonic, elastic tissues of a vigorous individual.

(III) *Increased permeability* of the capillary walls from chemical, physicochemical, and nervous causes (toxins, venous stasis, vasomotor relaxation).

(IV) *Impairment of the mechanism* of absorption; compression of the lymphatics from any cause; impairment of the endothelial cells.

(V) *Nervous influences* contribute powerfully to the production of œdema. This mode of action certainly exists, although we have no direct proof of it.

2. **Pathologic Physiology of Œdema.**—It is necessary to group the symptoms accompanying œdema into several groups:

(I) Those due to mechanical disturbances from the accumulated fluid: dyspnœa, compression of viscera, impediment to the movements of the lungs and especially of the heart.

(II) Those symptoms due to the underlying cause of œdema—*e. g.*, of nephritis, loss of cardiac compensation, latent uræmia and urinary poisoning, etc.

(III) Those due to the absorption of œdematous fluid: delirium, nervous excitement, sopor, etc. Lastly, we must bear in mind that death in cases of œdema, even of anasarca, is caused, as a rule, by the underlying cause or causes. Moreover, the morbid symptoms necessarily vary with the localization, the extent and variety of œdema, as well as with the general resistance of the individual.

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DIVISION *B.*

THE PHYSIOLOGY OF THE EXTERNAL RELATIONS: THE MOTOSENSORY ACTIVITIES.

Chapter IX. THE DERMAL SYSTEM: PROTECTION.
Chapter X. SENSATION.
Chapter XI. PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM.
Chapter XII. PHYSIOLOGY OF THE MUSCULAR SYSTEM.

CHAPTER IX.

THE SKIN: THE DERMAL SYSTEM.

INTRODUCTION.

1. SUMMARY OF THE MORPHOLOGIC FEATURES OF THE DERMAL SYSTEM. THE HISTOGENESIS AND HISTOLOGY OF THE SYSTEM.
2. THE GLANDS OF THE DERMAL SYSTEM.

THE PHYSIOLOGY OF THE DERMAL SYSTEM.

1. PROTECTION.
2. THERMOLYSIS.
3. EXCRETION.
4. RESPIRATION.

INTRODUCTION.

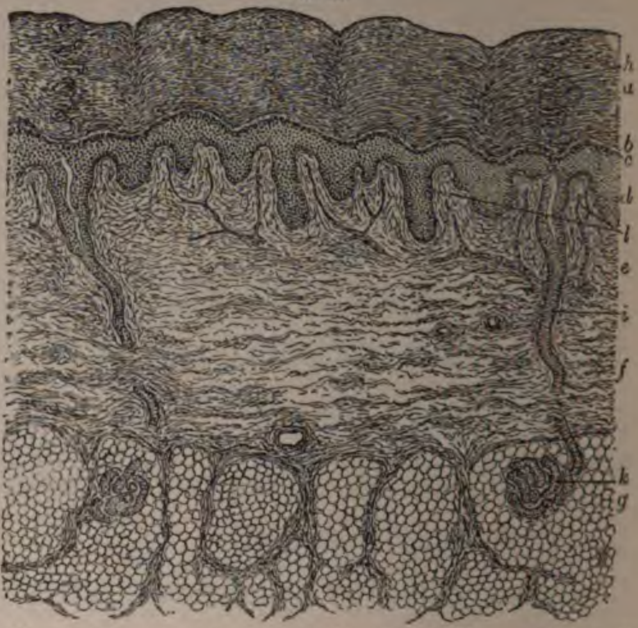
THE skin may be looked upon as an organ. Those structures intimately associated with the skin, both histogenetically and functionally, may, with the skin proper, be called the *Dermal System.*

This system of organs represents histogenetically epiblast proper and dermal mesenchyme; the former giving origin to those tissues and organs which are distinctively dermal, and the latter furnishing the substratum upon which these distinctive structures are built or supported. Functionally the dermal system is, *par excellence,* the system of *external relations,* which fact has a definite relation to the histogenesis, the epiblast coming from the ectoderm of the gastrula.

1. SUMMARY OF THE MORPHOLOGIC FEATURES OF THE DERMAL SYSTEM.

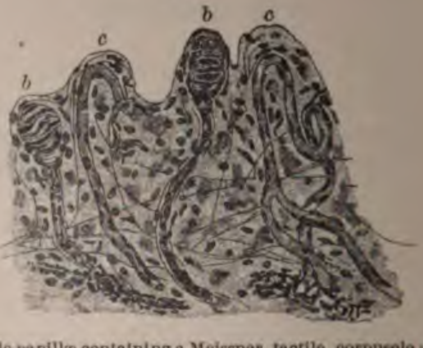
From a physiologic standpoint the following points regarding the structure of the skin and its associated organs are of importance:

FIG. 205



Section of human skin: *a*, stratum corneum; *b*, stratum lucidum; *c*, stratum granulosum; *d*, stratum Malpighii; *e*, *f*, papillary and reticular layers of corium; *g*, stratum of adipose tissue; *h*, *i*, spiral and straight portions of duct of sweat gland; *k*, coiled portion of sweat gland; *l*, vascular loops occupying papillæ of corium. (Piersol.)

FIG. 206



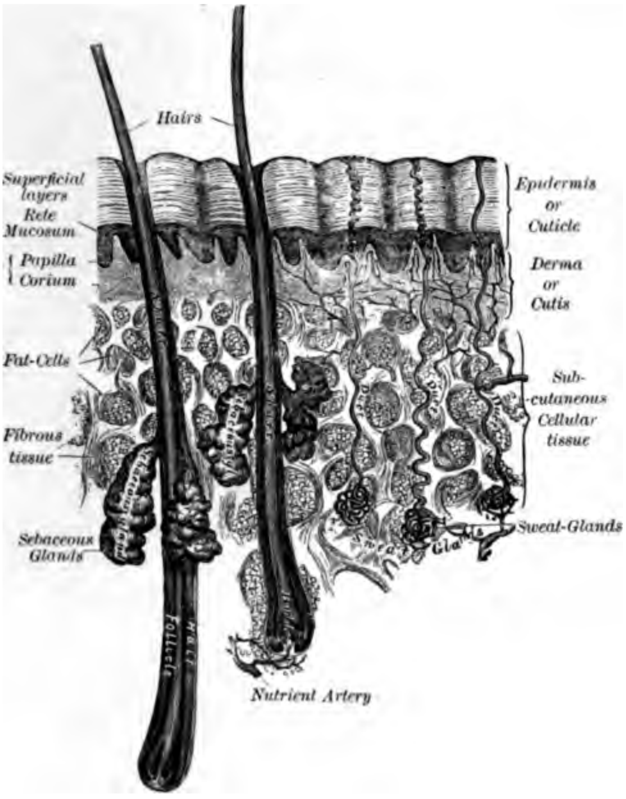
a, nerve fibre; *b*, tactile papillæ containing a Meissner tactile corpuscle; *c*, vascular papillæ. (After Benda.)

The dermal system of organs involves, without exception, (*a*) mesenchymal tissues as foundation, and (*b*) an epiblastic surface as superstructure.

a. The Dermis, or Corium.

The Mesenchyme may be represented by the close-felted corium with its bloodvessels and lymph vessels; by the dentine of a tooth, or by the dense transparent substance of the cornea. (See Fig. 205, *e*, *f*.)

FIG. 207



Section of the skin (diagrammatic). (Gray's Anatomy.)

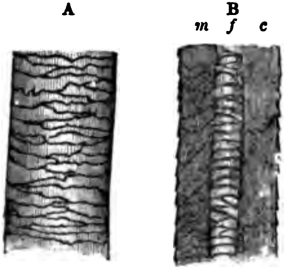
The mesenchymic dermis, or true skin, is everywhere beset with minute papillæ (Figs. 205 and 206). The papillæ are very vascular and through more or less specialized nerve endings they are especially sensitive (Fig. 206). These papillæ are variously modified in structure in different parts of the dermal system; they form the basis of a hair follicle; they form the basis of the nails and of teeth. Within them are located the special tactile corpuscles. In a further modification they form the lingual papillæ (*q. v.*). The marked vascularity of the papillæ facilitates the support of the tissues which are associated with them in the formation of hair, nails, teeth, etc. The nerve supply ensures the extreme sensitiveness of the dermal tissues enumerated—teeth, hair, nails—but it is the root or matrix which is sensitive, hair, not the nail, or tooth itself.

The epiblast may be represented by the cuticle of the skin, by the imbricated scales which compose a hair, by the active cells of the cutaneous glands, by the enamel of the teeth, or by the delicate cuticle which covers the cornea or the tympanic membrane. (See Fig. 205, *a*, *b*, *c*, *d*.)

b. The Epidermis.

The epiblast presents a series of layers whose cells are generated by karyokinesis at the surface of the corium from the columnar or cuboidal cells of the stratum Malpighii. The constant formation of new cells at this level pushes out the older cells which, through loss of water and through other physical and metabolic changes, die and become insensible, horny scales. The particular form and aggregation of these horny scales differ much in different locations. On the general cutaneous surface they are simply dry scales which are constantly shed; on the hair, teeth, or nails, there is an accumulation which takes a distinctive form and which serves as an organ of protection, defence or offence, and is only periodically shed or is worn off to keep pace with growth (or conversely). In the case of man the hair and nails are usually artificially cared for, the occupation of man not usually wearing the growth away fast enough.

FIG. 208



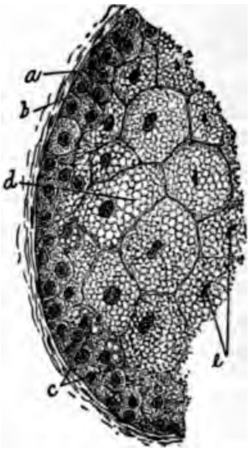
Piece of human hair. (Magnified.) A, seen from the surface; B, in optical section. *c*, cuticle; *f*, fibrous substance; *m*, medulla, the air having been expelled by Canada balsam. (Schafer.)

2. THE GLANDS OF THE DERMAL SYSTEM.

1. Protective Glands.—The Sebaceous Glands are present over the whole surface of the body except the soles of the feet, the palms of the hands, the dorsal surface of the third phalanges. (See Fig. 209.) The ducts of the glands open at the roots of the hairs on all hairy surfaces, but on the lips, the prepuce, and the corona of the glans penis the ducts open free upon the surface. The secretion of the sebaceous glands is called sebum.

Specialized forms of the sebaceous glands are: (1) *Preputial glands*, whose secretion—the *smegma preputii*—differs from sebum in containing substances which give it a characteristic odor. Musk is from the preputial gland of the musk deer. (II) *Anal glands*, which are only slightly modified in the human subject, may be strongly modified in other mammalia. In the otter, hyena, and civet the anal glands secrete a modified sebum which serves for sexual attraction. In the skunk the secretion serves for defence. (III) The *Meibomian glands* are slightly modified sebaceous glands which open upon the edge of the eyelid; the oily surface thus produced prevents the overflow of tears. (IV) *The Uropygial Gland* of birds is a specialized sebaceous gland. The oil which it secretes is spread upon the feathers by the bird and serves to protect the feather-coat against absorption of water. (V) *The Lacrymal Gland*, whose secretion keeps the delicate mucous membrane of the conjunctiva moist and freed from dust, belongs to the dermal system and to the protective glands of that system, though morphologically they are more closely related to the salivary glands.

FIG. 209



Section of portion of sebaceous gland from human scalp, including part of the acinus: *a*, membrana propria; *b*, peripheral layer of cuboidal cells; *c*, elements in which fatty metamorphosis is beginning; *d*, cells filled with fatty particles and exhibiting marked intracellular networks; *e*, nuclei of cells. (Piersol.)

2. **Secretory Glands.** — The mammary glands, unquestionably dermal glands, may have been derived phylogenetically from sweat glands. The secretion formed and the method of its formation make the lactiferous glands clearly analogous (if not homologous) to the sebaceous glands. (See *Lactation*, under *Reproduction*.) Pigeons possess lactiferous glands which are clearly sebaceous glands and are tributary to the crop. This "pigeon milk" contains fat, a protein clotting with rennet, globulin, salts, and water.

3. **Excretory Glands.**--The sweat glands (Fig. 207). See Cutaneous Excretion, page 529 *et seq.*

THE PHYSIOLOGY OF THE DERMAL SYSTEM.

1. PROTECTION.

The skin, being the organ of external relations, must necessarily stand between the general organism and its environment.

a. The Nerves of the Skin.

The skin is provided with sensory nerve ends; this tends to protection in putting the animal on guard against various dangers.

Some of these sensory areas are highly specialized—*e. g.*, the cornea and lens admitting light to the retina; the taste buds—facilitating the access of solutions to the gustatory nerves; the moist nasal epiblast facilitating the influence of odors upon the olfactory nerves.

b. Dermal Protective Structures.

The skin is provided with various structures for special protection against mechanical injury—*e. g.*, the nails protect the finger-tips and toe-tips; hair protects the organism against mechanical injury —witness its cultivation for that purpose by football players—it serves a more important office, however, in protection against cold. In this connection may be mentioned the further protection of the eye by the lids whose periodical winking during working hours and continued closing during sleeping hours serve to protect the eye against dust and drying. The eyelashes protect the eye against bits of solid matter that might otherwise strike the eye. The brows shed off the perspiration. All of these protective structures are dermal. The teeth are, however, more distinctly prehensile and offencive than defencive; though the dermal teeth of sharks are defencive and protective and the oral teeth are the homologues of the dermal teeth.

c. The Sebaceous Glands.

The skin is provided with oil glands or sebaceous glands whose function is to secrete oil for the hair and cuticle, keeping both soft and pliable and especially non-absorbent. As indicated in the introduction, the oil glands may take various specialized forms, as for offence, defence, or sexual attraction. The chemical composition of the sebum is not very well known, because the normal cutaneous secretion is not formed in sufficient quantity for analysis. The cheesy contents of a distended sebaceous cyst consist of water 31.7 per cent., epithelium and nucleoalbumin 61.7 per cent., fat 4.2 per cent., fatty acids 1.2 per cent., salts 1.2 per cent. In the typical secretion the proportion of fat and fatty acids is probably much greater, and that of epithelium and nucleoalbumin much smaller. The *fat* consists of a mixture of *glycerin fats,* with whose composition the reader is familiar, and of *cholesterin fats.* Cholesterin is a monatomic alcohol having the formula $C_{27}H_{45}OH+H_2O$. Cholesterin fat of palmitic acid is $CH_3—(CH_2)_{14}—COO{\cdot}C_{27}H_{45}$. The *fatty acids* consist, according to Schmidt, of butyric, valeric, and caproic acids. It is to the fatty acids that the secretion owes its distinctive odor. Free *cholesterin* and isocholesterin are present.

Two especially interesting facts regarding the sebum are: First, *the cholesterin fats resist putrefaction*—i. e., *they resist the use of the skin as a culture field for bacteria.* Second, the homology of the mammary glands with the sebaceous glands receives an extra element of probability in the fact that the *nucleoalbumin of the sebum is casein.*

2. THERMOLYSIS.

The common cutaneous surface, with its vascular cutis vera and its sweat glands, forms the *organ* of *Thermolysis.* Just how the skin governs the rate of heat elimination is discussed in full under Animal Heat.

3. EXCRETION.

Third in importance among the functions of the skin is excretion. Here is an instance where an excretion performs an important office incident to its final exit from the body. Every gram of water which evaporates on the surface of the skin eliminates 582 calories of heat, or takes that much away from the body.

It is evident that *Excretion* and *Thermolysis* are intimately associated. The greater the occasion for free evaporation of water incident to thermolysis, the greater the excretion of water by the skin. But if there is a given amount of water to be eliminated from the system, it is evident that the other water-eliminating organs must give off correspondingly less water. Such is the case; after profuse perspiration the urine is less voluminous and more highly colored. Conversely, a marked decrease of perspiration will be occasion for a marked increase of the volume of urine, which will be more watery. Not only is there a *reciprocity,* there is also a vicarious relation between skin and kidneys. When one is disabled the other performs as much as possible of the function of the disabled organ.

4. RESPIRATION.

In many of the lower animals, particularly in amphibia, the skin is an important organ of respiration. The moisture of its surface facilitates the exchange of gases by diffusion in these animals.

In the higher vertebrates respiration is an unimportant function of the skin.

CHAPTER X.

SENSATION: INTRODUCTION.

A. GENERAL SENSATION.

1. SUBJECTIVE.
2. SUBJECTIVE-OBJECTIVE.
    - COMMON SENSATION.
        - (*a*) *Hunger.*
        - (*b*) *Thirst.*
        - (*c*) *Suffocation.*
        - (*d*) *Fatigue.*
        - (*e*) *Pain.*
        - (*f*) *Shivering*
        - (*g*) *Tickling.*
        - (*h*) *Sexual Sensation.*
3. OBJECTIVE.
    - I. THE TACTILE OF PRESSURE SENSE.
    - II. THE POSTURE SENSE.
        - (*a*) *Sense of Equilibrium.*
        - (*b*) *Muscular Sense.*
    - III. THE TEMPERATURE.

B. SPECIAL SENSATION (OBJECTIVE): THE SPECIAL SENSES

- IV. SMELL.
- V. TASTE.
- VI. HEARING.
- VII. SIGHT.

INTRODUCTION.

EVERY animal organism is provided with organs which make the cerebral sensory centres cognizant of certain conditions and changes of the environment. In other words, certain conditions of the environment act as stimuli to more or less specialized peripheral organs. The effect of a stimulus is transmitted along an afferent nerve to the brain, where it so affects the cerebral centres as to cause a consciousness of the stimulus—*a sensation*. Through inter-central action between the sensory centres and the higher cerebral centres the animal sums up the sensations received from an object making a complete conscious *perception*. An interpretation of perceptions producing not only a mental picture of an object and its properties, but giving the animal an idea of the relation of the object under consideration to other objects, is called a *conception*.

ɔte that a conscious sensation involves *attention;* that perception ves *memory;* and that conception involves *reason.* The clearness ıe sensation, perception, and conception is proportional to the ıtion, memory, and reasoning involved in them. *Sensation ishes the foundation for all higher forms of mental activity.*

ıe ectoderm is the embryonic layer which gives rise to the per-ral organs of sensation as well as to the sensorium. The special-epithelium of the sense organs is from the epiblastic division of ectoderm, while the sensorium is from the neuroblastic division at layer.

will be profitable at this point to express in tabulated form the ions between the specific stimuli of the environment, the more or specialized peripheral sense organs which receive the stimuli and pecial sensations aroused in the sensorium.

owing Relations between Stimuli, Sensory Nerve Endings, and Sensations.

	General Stimuli.	Special Stimuli.	Sensory Nerve Endings.		Sensation.
ions be on- it					A. General Sensation.
	Mechanical	Pressure Tension	Filamentous endings.		*Auto-objective sensation.* a. Hunger. b. Thirst. c. Suffocation. d. Fatigue. e. Pain. f. Shivering. g. Tickling. h. Sexual sensation.
	Thermal	Heat.	Tactile cells	Simple compound or corpuscle of Grandry	
			Tactile corpuscles	Spherical end bulbs Genital corpuscles Meissner's corpuscles	*Objective sensation.* I. Tactile or pressure sense. II. Posture sense. a. Muscular sense. b. Sense of equilibrium. III. Temperature sense.
			End bulbs	Cylindric end bulbs Pacinian corpuscles	
					B The Special Senses.
	Chemical	In gaseous medium	Olfactory nerve endings		IV. Smell.
		In liquid medium	Gustatory nerve endings		V. Taste.
	Vibration of ponderable matter	Sound	Auditory nerve endings: organ of Corti		VI. Hearing.
	Vibration of imponderable matter	Light	Optic nerve endings: retina		VII. Vision.

ɔte that there is a departure from the time-honored classification e senses as: "Five: Feeling, taste, smell, hearing and seeing."

The first one of these has, under careful investigation, been resolved into several distinct senses, one classification of which is given in the table.

Sensory nerve endings may be classified, on the basis of structure, into specialized and non-specialized. The specialized nerve endings—those enumerated in the table below the dash—are those which seem to be especially adapted structurally for response to particular stimuli. For example, the structure of the retina, exceedingly complex and highly specialized, seems to be especially adapted to receive the light, while the organ of Corti, just as complex, seems to be especially adapted to receive sound. Moreover, the retina is sensitive to light only of all the stimuli of the environment, or if there is a response to any other kind of energy it always affects the sensorium as light. In the same way sound alone of all the stimuli of the environment affects the organ of Corti. Another structural distinction is found in the fact that the specialized nerve endings are all located in particular organs also especially adapted to receive the special stimulus; for example, the refractive media of the eye focus the light upon the retina, and the muscles of the eye direct the organ toward the source of light. The non-specialized nerve endings are more or less widely distributed over the surface of the skin and mucous membranes. They are not located in specialized organs and are not evidently adapted to receive special stimuli. It may be that the "tactile cells and corpuscles" are the end organs of *touch and muscular sense*, and it may be that the filamentous endings or the end bulbs are the end organs of the temperature sense; but these distinctions, if they exist, remain yet to be demonstrated.

Sensations may be classified into three categories on the basis of the source of the stimulus:

1. Sensations which are the immediate result of the reaction of the organism to the conditions of the environment: pressure sense, posture sense, temperature sense, smell, taste, hearing, vision. Because these sensations are caused by objects wholly outside of the organism they are called *Objective Sensations.*

2. Sensations in which the immediate source of the stimulus is within the organisms, though the ultimate source is in the environment. An example of this class of sensations is *hunger.* Something within the organism produces a conscious call for nourishment. This may be so urgent as to occasion considerable discomfort, merging into actual pain if not satisfied. The ultimate cause of hunger is in the environment, but the stimulus cannot be classified with the general or special stimuli enumerated in the foregoing table.

Thirst and *fatigue* also belong clearly to this class of sensations. *Pain* and *sexual sensations* may belong to this class or to the preceding. In these two sensations the stimulus may be mechanical and may be traced more or less immediately to the environment. This class of sensations may, for want of a more concise term, be called *Auto-objective Sensations.*

3. Sensations which accompany dreams, hypnosis, hysteria, and various states of the central nervous system, and which merge from the perfectly normal into the pathologic. These sensations are just as real to the subject as are the objective sensations, but an observer traces no connection to an external stimulus, or any condition of the environment. Such sensations are called *Subjective Sensations.* They partake of the nature of a memory of previous sensations, but they are more than that. A subjective sensation is an actual *re-experiencing of a former sensation.*

THE PHYSIOLOGY OF SENSATION.

A. GENERAL SENSATIONS.

The term general sensations is used to include a class of sensations excluded by the well-defined *special senses*—*i. e.*, the general senses are those with no specialized peripheral organs.

1. SUBJECTIVE GENERAL SENSATIONS.

This class of sensations has been sufficiently discussed above.

2. AUTO-OBJECTIVE SENSATIONS.

For the definition of this class see the Introduction.

a. Hunger. *b.* Thirst. *c.* Suffocation.

These three sensations are nature's admonitions to supply the organism with solid, liquid, or gaseous nourishment. The greater the urgency for satisfaction of the need, the greater the discomfort when it is not satisfied. The animal organism can live only a short time without oxygen. When the supply of oxygen is cut off the sensation of suffocation begins within a few seconds and increases rapidly in intensity, passing very soon into a paroxysm of the most agonizing pain, ending in convulsions and death if the need is not supplied.

Next to oxygen in urgency is the need for water. If there is little perspiration the thirst may be mild for twenty-four hours. As soon as the sensation of thirst becomes thoroughly fixed upon the consciousness of the animal nothing can dislodge it. The discomfort becomes more and more intense until death supervenes.

The animal organism can do without food for many weeks if all activity can cease. Bears hibernate for several months. Indians accustom themselves to forty-eight-hour and seventy-two-hour fasts in order to be able to endure without much discomfort the exigencies of war and the chase. To those who are accustomed to three regular meals each day the missing of one meal is likely to cause considerable discomfort, but the feeling is one of emptiness rather than of real hunger. If one fill the stomach with water the discomfort soon disappears and real hunger begins to appear in a variable time afterward. Hunger and thirst are in the healthy individual infallible signs of the needs of the organism. These senses may, however, become perverted, or, at least, the actual sensation may be misinterpreted. For example, a child with an overfilled stomach may call for more—having misinterpreted the vague feeling of discomfort in the gastric region for hunger.

d. **Fatigue.** *e.* **Pain.**

These two sensations apprise the organism of overstimulation. Moderate overstimulation is followed by a feeling of fatigue. Nature is requesting a rest. Excessive overstimulation leads to a feeling of actual pain. Nature is *demanding* a rest. The most usual occurrence of weariness is after muscular or nervous activity; the most usual occurrence of pain is after stimulation of some of the peripheral end organs by some of the external stimuli: pressure, tension, heat, cold, chemical energy, sound or light. But pain may be a purely subjective sensation, having no apparent connection with objects outside of the organism, but arising from certain conditions in the central nervous system. Some painful sensations may be accurately localized, while others are localized in a most general way only. The more acute the tactile sense of a part, the more accurate the localization of pain in the part. Pain is the most general of all sensations. Some contend that there is a special set of nerves to convey the sensation of pain together with certain other sensations. But the fact that every sensation of which the brain may be conscious and every activity of which the organism is capable may be accompanied by pain, and the fact that abnormal conditions of the system may be accompanied by pain, make it highly improbable that any particular set of nerves is to be looked upon as pain nerves.

f. **Shivering.** *g.* **Tickling.** *h.* **Sexual Sensation.**

These sensations have certain features in common. They all begin in definite objective sensations and partake of the nature of *after-sensation.* If the cold points of a considerable area are stimlated so that the superficial tissues become chilled, the shivering nsation is induced. Once started, it is likely to continue some time fter the local reaction has occurred. Moreover, the sensation equently occurs when there is no objective cause—*i. e.*, it may ave its origin in the central nervous system. Tickling sensation usually caused by a light stimulation of the tactile nerve endings, ut in many individuals the sensation may be aroused by "make-lieve" movements on the part of another, or even an active imagiation may induce the sensation. Tickling may have its origin in e central nervous system. Sexual sensation may be stimulated ripherally by mechanical stimuli, or centrally. In fact, the most fective stimulus is the central one. If the stimulation be carried to e point of the final, culminative sensation (orgasm), this is to be oked upon as the *indirect after-sensation* and not the *direct objective nsation*, and it is the indirect after-sensation which belongs to the tegory of the heading.

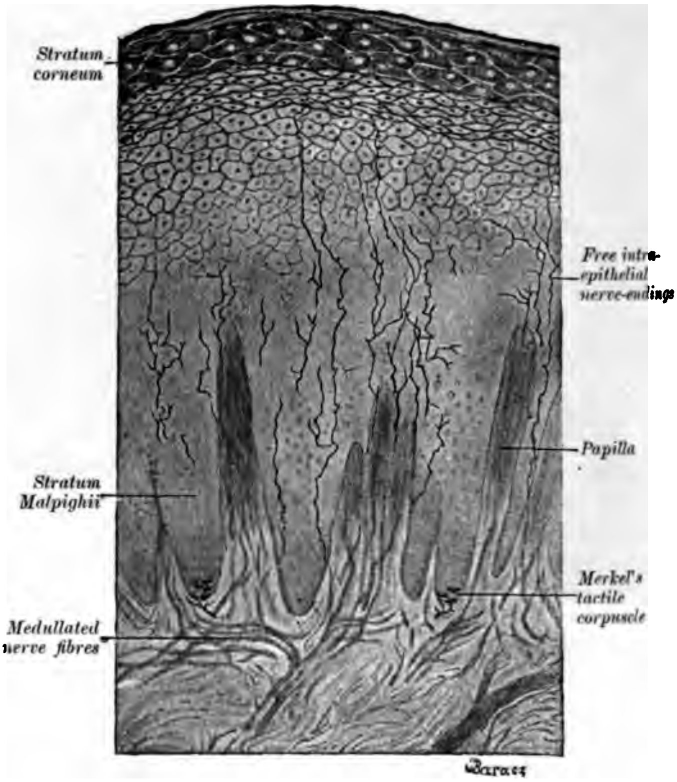
3. OBJECTIVE SENSATION.

Preliminary to a discussion of the general sensations of the periphery ne may profitably review the structure of the sensory nerve endings. hese endings may be classified as simple and complex. The simple re called *filamentous* and are distributed to the skin, cornea, mucous embranes, and tendons. (See Fig. 210.) *The complex sensory nerve dings* represent three genera: tactile cells, tactile corpuscles, and d bulbs. Figure 211 represents *tactile cells.* The tactile cells iffer from the filamentous endings in having a discoidal termination sociated with a slightly modified epithelial cell. Another form of ctile cell lies within the epidermis of the mammalian or avian skin. ote the disks and the two or three cells enclosed in a sheath.

The *tactile corpuscles* are located in the corium of skin and mucous embrane. The *spherical end bulbs*, shown in Fig. 212 are found the conjunctiva and other mucous membranes of man. *The genital rpuscles* are found upon the glans penis, the glans clitoris, and other sociated surfaces in mammals in general. The *tactile corpuscles* of eissner are located in papillæ of the corium upon the palms of the ands, the soles of the feet, and upon the volar surfaces of fingers and es in man. The complex internal structure of these bodies is shown Fig. 213. There can be little doubt that these specialized sensory erve endings are the organs of touch, if it is admissible to call them rgans. Of the several species of end bulbs only one will be given—*e Pacinian body* (Fig. 214.) These structures are widely distribted in mammals. They occur in subcutaneous tissue along the erves supplying the skin, especially of the hands and feet, the xternal genitalia, the joints of the extremities, periosteum of certain ones, and the peritoneum.

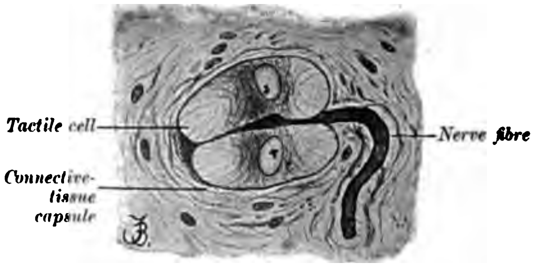
The various structures just described receive at the peripher various sensations. The fact that the tactile corpuscles of Meissne

FIG. 210



Filamentous nervous fibres of epidermis. (Szymonowicz.)

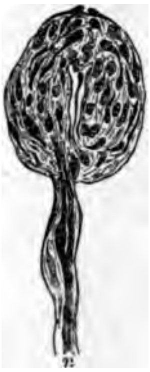
FIG. 211



Tactile cells with capsule. (Szymonowicz).

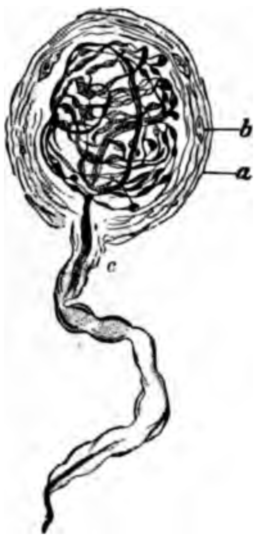
are most numerous in those locations where the tactile sense is m acute justifies the conclusion that these structures represent periphe nd organs for mechanical stimuli, but does not justify the conclusion hat none of the other sensory-nerve endings respond also to various nechanical stimuli. It is probable that some of the endings described espond to mechanical stimuli and some to thermal. The mechanical timuli may be further subdivided; some of them in the form of ressure affect the cutaneous and articular surfaces, while others in he form of varying tension affect the tendons and muscles. The hermal stimuli are also to be ubdivided: bodies lower in temerature than the skin stimulate ertain nerve endings, while bodies f higher temperature stimulate ther nerve endings. Whether ese nerve endings differ from ch other structurally as well as functionally or differ only functionlly is unknown. In short, the sensations classified in the above table . 551) are the result of the stimulation of some one or more of the nsory nerve endings enumerated in the opposite brace; this is all at can be said with certainty at present.

FIG. 212



Simple spherical end bulb from the human njunctival mucous membrane: *n*, the meillated nerve fibre which disappears within e capsule. (After Krause.)

FIG. 213

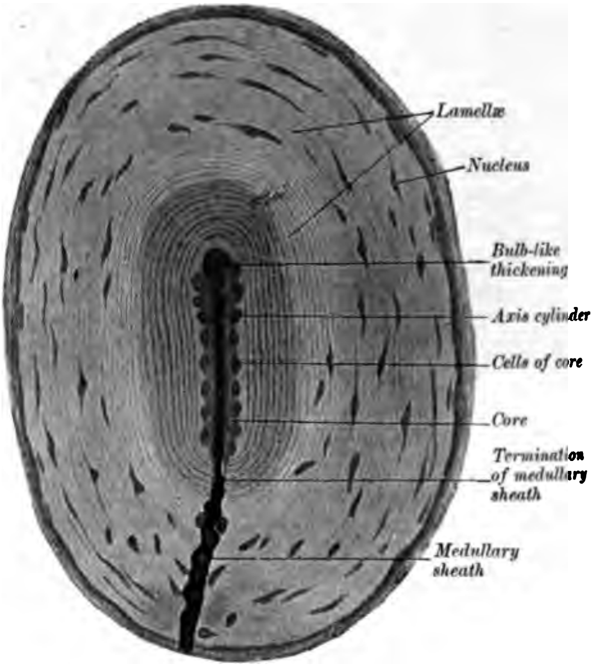


Meissner's corpuscle from human corium. *a*, upper portion, in which the epithelial cells alone are represented. The nuclei of these cells are in the broader peripheral portion of the cytoplasm. *b*, nerve dendrite coiled about the epithelial cells; *c*, nerve fibre. (Böhm and Davidoff.)

I. THE TACTILE SENSE: THE SENSE OF TOUCH.

In man this sense is most acute in the finger-tips, the lips, and he tongue. In quadrupeds the sense is most acute in the lips, ongue, or proboscis. This sense alone brings to one only an idea f the state of the substance—whether it is solid, liquid, or gaseous; f the surface of a solid—whether it is smooth or rough, and if the latter the particular character of the roughness; whether it is oily or sticky, or whether it is bounded by curved surfaces or by planes, edges, or angles, or a combination of these features. The character of a liquid may be determined, whether it is light, limpid like water, or heavy like mercury, or whether it is gelatinous, viscous, slimy, or oily. The only character of a gas that appeals to the tactile mechanism is the negative one that it affords no resistance to the movements of hands or fingers. The sum of the knowledge which may be derived through touch alone is greater than that which may be derived through any other one sense. Experience derived from both touch and sight will enable one to *infer* from lights and shades and lustres what touch would definitely reveal. One instinctively verifies these inferences by touching the object with the fingers.

FIG. 214



A Pacinian corpuscle from the mesentery of the cat. (Szymonowicz.)

The tactile sense is used in two different ways: first, to announce to the central nervous system when some resistant object touches the surface of the body; second, to investigate the properties of certain objects of the environment. In the first the organism is passive; in the second it is active. The first is a means of protection, the second a means of adding to one's knowledge. A similar classification of function may be made for all of the objective sensations. In serving ɜ first one of these purposes the tactile mechanism must be able to ferentiate stimulation of different portions of the periphery. It not enough to know that some sharp point is touching the surface the body, but to avoid injury it is important to know just where ɜ point is. This is accomplished by what is called the *power of alization.* Through this power the central nervous system is nscious—*e. g.*, that in a particular location a sharp point is touching ɜ periphery. This knowledge enables the organism to protect itself m unnecessary injury. The tactile mechanism is also endowed th the *power to estimate pressure.* Those portions of the skin most ute in their tactile sensibility are, at the same time, most acute their power of localization, but not in their power to estimate press- e. This has led to two methods of testing the tactile sense: one measure the power to estimate pressure, and the other, the power localization.

To test the pressure sensibility one places upon a certain cuticular ea a series of weights of exactly the same surface of contact and proximately the same temperature. Such experiments have vealed the facts that the parts most sensitive to pressure are the rehead, the temples, the back of the hand, and the flexor surface the forearm. In these localities 2 mgm. can be felt, while the ger-tips cannot feel a weight of less than 5 to 15 mgm.

Regarding the power to differentiate increments in the weights ed as stimuli it may be said that: *the greater the initial stimulus the eater the increment must be in order to be discernible.* This is the sis for Weber's law: "*The amount of stimulus necessary to provoke perceptible increase of sensation always bears the same ratio to the nount of stimulus already applied.*" Fechner studied this same oblem and reached similar results, which he formulated in his psychophysical law": "*The intensity of sensation varies with the garithm of the stimulus.*" That is, if a series of stimuli represent e intensities 10 : 100 : 1000 : 10,000, the sensations would represent e intensities 1 : 2 : 3 : 4. These laws hold in the main for medium imulation; for very light or very strong stimulation they do not hold, e *sensation being more acute for moderate stimuli.* Another law of eber[1] may be thus formulated: *If two equal weights have different eas of contact, the one that touches the larger surface feels the avier.*

The acuteness of touch and the power of localization is tested by use the æsthesiometer, which is similar to a pair of dividers or to a aughtsman's compass. In using the instrument the points are lightly uched to the surface of the skin. The greater the acuteness of ctile sense, or the more acute the power of localization, the nearer e points may be brought together and yet be felt as two points.

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[1] Hermann's Handbuch der Physiologie, Bd. iii. 2, S. 336.

Beyond a certain minimum distance the points can no longer be distinguished as two, but feel like one point.

The following table shows results of tests which were made to determine whether all points are equally sensitive and especially whether symmetrically located points on the same individual are equally sensitive.

Showing variations of symmetrically located points on the same individual. From this table one is justified in three inferences:

1. Symmetrically located points in the human body may not possess the same acuteness of tactile sensation.
2. There is a very great variation in the acuteness of sensation in different parts of the cutaneous surface of the same individual.
3. The more acute the tactile perception of a part, the more likely it is to vary in acuteness from its laterally homologous point.

TABLE I. OF TACTILE SENSIBILITY.

Point of Observation.	Individual A.		Individual B.	
	Right.	Left.	Right.	Left.
Tip of Tongue.	1.2 mm.	1.2 mm.	1.2 mm.	1.2 mm.
Palm of 3d Phalanx.	2.0	2.5	2.00	1.5
" " 2d "	3.75	3.25	3.5	3.5
Tip of Nose.	5.5	5.5	8.0	8.0
Back of 2d Phalanx.	9.0	11.0	9.9	8.0
Back of Hand.	15.0	20.0	17.0	22.0
Forearm.	24.0	24.0	42.0	42.0
Sternum.	32.0	32.0	42.0	42.0
Back.	66.0	66.0	77.0	77.0

Tests upon a number of individuals yielded the results recorded in Table II., showing not only the variations of tactile sensibility in different parts of the same individual, but also the variations of different individuals.

TABLE II.

)EGREES OF TACTILE SENSIBILITY OF CUTANEOUS SURFACE OF BODY.

Portion of the Body Tested.	Man. mm.	Boy æt 18. mm.	Woman. mm.	Man. mm.
ongue.	.7	1	.6	.8
of dorsum of tongue.	1.1	1.1	1.	1.6
of hard palate.	1.6	4.	2.3	1.1
ip (red surface).	7	2.1	1.7	2.1
ip (" ")	1.3	1.2	1.5	3.
iose.	4.	2.	1.2	2.5
hin.	5.	6.	6.	2.8
ver malar bones.	5.	4.	4.	6.5
ear (ventral surface),	4.5	6.7	3.2	5.6
entral surface).	3.	4.1	3.1	5.8
lorsal surface).	2.2	3.7	1.8	5.4
ateral surface).	2.2	3.2	2.9	5.4
d.	5.1	4.9	4.3	5.2
fingers.	1.	1.1	1.4	1.
surface of second phalanges of fingers.	1.1	2.	3.8	1.6
" " " " " " (transverse).	5.	3.2	3.6	1.1
" " " " " " (longitudinal).	7.5	3.	6.1	5.
surface of hand.	2.1	3.2	4.2	2.3
hypothenar eminences.	.8	2.1	4.2	2.2
of hand (longitudinal).	5.6	4.3	6.5	3.6
urface of forearm.	5.7	4.5	5.3	5.
" " upper-arm.	4.8	4.7	5.8	5.2
of hand (transverse).	4.7	2.8	4.2	6.
surface forearm.	3.3	3.2	4.5	2.8
surface upper-arm.	5.8	4.7	4.5	1.7
of foot.	12.	15.	19.	24.
surface of thigh (transverse).	36.	30.	34.	33.
leg.	15.	28.	21.	30.
dorsal region.	38.	35.	37.	40.
sacral "	30.	28.	31	32.
cervical region.	35.	32.	39.	37.
ral region (over spine).	18.	16.	13.	15.
sal " " "	10.	13.	17.	11.
vical " " "	12.	14.	15.	10.
surface thigh (longitudinal).	64.	57.	61	69.

II. justifies the following conclusions:

re is very great variation in the acuteness of perception in parts of the same individual.

re is considerable variation in the acuteness of tactile per-n different individuals.

en the points determine a line which is transverse to the limb they may be distinguished as TWO at a much smaller than is the case when the line is parallel to the axis of the

tactile sense is best developed in persons whose senses in re well developed: for example, Mr. Z., a laboring man, pared with Miss X. in twelve points of observation, and rmly excelled him. But not in tactile sense alone did excel Mr. Z. Her sense perceptions in general were more

farther one goes from the tips of fingers, toes, or tongue cute is the tactile perception.

least sensitive parts of the body are those subject to more onstant pressure; the epidermis is, in such locations, very

7. The tactile sensibility is much more acute on all flexor surfaces than upon the corresponding extensor surfaces. For evidence see Table III.

TABLE III.

Flexor Surfaces.		*Extensor Surfaces.*	
Over Pectoralis Major.	20 mm.	Over Scapula.	32 mm.
Umbilical Region.	18 "	Dorsal Region.	53 "
Neck (ventral).	11 "	Neck (dorsal).	15 "
Arm.	15 "	Arm.	17 "
Forearm.	7 "	Forearm.	11 "
Wrist.	7 "	Wrist.	9 "
Thigh.	45 "	Thigh.	53 "
Leg.	9 "	Leg.	15 "
Average.	16.5		25.6

II. THE POSTURE SENSE.

The organism is provided with a mechanism through which it is made continually conscious not only of the general position of the body in space, but of the relative position of different parts of the body. The consciousness of general position in space is called the sense of equilibrium; the consciousness of the position of different parts of the body is inseparable from muscular sensation, and is probably incidental to it. These two sensations together give the organism a clear consciousness of its position or posture—*i. e.*, gives the *Posture Sensation.*

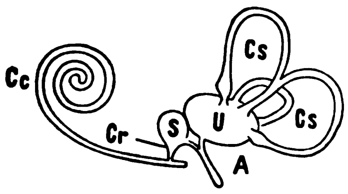
a. The Sense of Equilibrium.

The maintenance of equilibrium is of prime importance both in animal locomotion and in all positions of rest, except that of absolute relaxation in a recumbent position. The whole mechanism of equilibrium includes the nicely adjusted muscular action required to hold head and body poised upon the base of support, and it includes the sensation necessary to make the central nervous system cognizant of any disturbance of the poise. This sensory part of the mechanism is the one now under consideration. The principal end organ of equilibrium seems to be the system of semicircular canals connected with the inner ear. If this were the only end organ the sense of equilibrium might probably be classed as a special sense. But the complete sensation of equilibrium is a combination of sensations from various sources; it might, in fact, be called, rather, a *perception of equilibrium,* rather than a simple sensation. (See Introduction, p. 550 *et seq.*) The sensory nerves from the soles of the feet (from the ischial skin when sitting), from the muscles and tendons, from the articular surfaces, and from the eyes all bring sensations which contribute to the general sensation or *perception of equilibrium.* If any part of the mechanism is disabled the equilibrium is in part impaired. The parts intact may by especial activity cover the deficiency in the mechanism, but though the maintenance of equilibrium may be apparently perfect the sense of equilibrium is not perfect.

In this place we may discuss those features of the semicircular canals, which especially fit them for end organs for the perception of the position of the axis of the body in space. Fig. 215 shows the membranous labyrinth with its three canals, two saccate structures, and the cochlea. Note (I) that each canal has an enlargement near one end—the ampulla; (II) that the three canals lie in different planes.

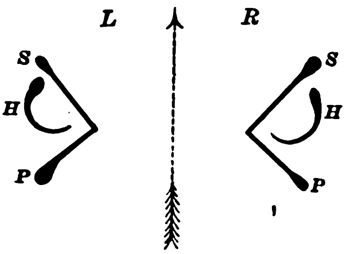
Fig. 216 gives Waller's diagram showing certain important space relations of the canals. Note (III) that the superior canal of the right side lies in a plane parallel to that of the posterior canal of the left side, while the left superior plane is parallel to the right posterior plane, and the two horizontal planes are parallel; (IV) that the six planes represent the three dimensions of space; (V) that the ampullæ of any pair of parallel canals are at opposite extremities of the canal —*e. g.*, the ampulla of the left superior canal is opposite to the ampulla of the right posterior canal. Each ampulla contains a ridge (crista acustica) surmounted by long, delicate bristles which are epiblastic in their origin. These bristles are borne by specialized epithelial cells each of which is intimately connected with a branch of the vestibular nerve. The bristles are really agglutinated structures, each formed of several fibrillæ. The saccule and the utricle are each provided with a small specialized surface similar to that of the crista.

FIG. 215



Membranous labyrinth: *Cs*, semicircular canal; *U*, utriculus; *S*, sacculus; *A*, aqueduct of vestibule; *Cr*, ductus reuniens; *Co*, cochlea.

FIG. 216



Diagrammatic horizontal section through the head to illustrate the planes occupied by the semicircular canals. (Waller.)

If the head or the whole body be rotated upon its anteroposterior axis in the direction from left to right, the endolymph of the right horizontal canal will flow toward the ampulla of the canal where the pressure would increase, while the endolymph of the left horizontal canal will flow away from the ampulla of that canal, tending to decrease the pressure. According to the hypothesis of Crum-Brown, fairly confirmed by experiment, this difference of pressure is the efficient stimulus. Other movements of the head, or of the body as a whole, affect other pairs of semicircular canals in a way similar to that indicated above.

Through this mechanism and its centre in the cerebellum the individual is made conscious of every position and every change of position of the head in space. If, in an animal, one of the semicircular canals be opened, the animal has the sensation which accompanies fall of pressure in that canal, and makes efforts to compensate it by "*forced movements*," which really carry the animal's body in the direction opposite to that in which it feels it is turning. Such observations have seemed to confirm the hypothesis of Crum-Brown, which is now generally accepted. Lee[1] looks upon the saccule and utricle as the organs of *static equilibrium*, in which, when the animal is at rest, the weight of the otoliths under gravitation stimulates the maculæ acusticæ. The fact that in fishes these structures are highly developed seems to confirm Lee's hypothesis, for in these animals there is no supplementary cutaneous stimulation like the solar or ischial stimulation in man, and the fish must depend entirely upon these structures for its sense of position.

b. The Muscular Sense.

Supplementary to the sense of position in space is the sense of muscular tension. If one stand erect and as still as possible with the heels together he will not be conscious of any essential change of equilibrium, yet he will be conscious of a slight variation of the distribution of weight upon the soles of the feet, and especially conscious of variation in tension of different sets of muscles and tendons involved in the maintenance of the erect position. If one fix a tracing point to the head and stand under a horizontal tracing surface, so adjusted as to record any change of position, it will be noticed that the position of the point changes from moment to moment—never returning exactly to the starting point except sometimes by accident. As a general rule, the taller the subject the greater the amplitude of his oscillations. A study of these tracings and of the sensations which one experiences while standing erect indicates that such a position is maintained particularly through the muscle sense. One is conscious at one time of a greater tension upon, say, the muscles of one side of the body than upon those of the other, and is conscious at the same time of a slight change of the direction of the body axis. A moment later he is conscious of a greater tension upon the sets of muscles which before were less tense and conversely. The muscles are in a state of mild tonic contraction constantly, but he tension of any one group of muscles varies continually, the action being so co-ordinated as to maintain the body erect within very narrow limits. One has not the sensation of losing and regaining the balance, but he has the sensation of shifting of pressure upon the oles of the feet, also of changing of tension in muscles and tendons. t may be said that *the coarse adjustment of equilibrium is effected hrough the semicircular canals, while the fine adjustment is effected hrough a combination of muscle sense and plantar reflex.*

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[1] Journal of Physiology, vol. xvii. p. 192.

Besides the important part which the muscle sense plays in the maintenance of equilibrium it serves the organism *in adjusting all motor activities to the required conditions.* The consciousness of a ertain amount of tension upon muscles or tendons seems to be he thing which governs the amount of energy liberated in the muscle o accomplish a subsequent similar act. Everyone has experienced he surprise and awkwardness in co-ordination which is likely to occur when in a flight of stairs one step is much lower than the others. The usual energy and space adjustment has been ordered in the entral nervous system in response to previous muscular sense. The new conditions take the nerve muscle system by surprise. This is not the case when the vision supplements the other equilibration apparatus. If one sees an unusual step he voluntarily modifies the ourse of the reflexes.

In common with other senses it may be much improved by practice. Experienced produce dealers can estimate with astonishing accuracy a particular weight of any commodity.

III. THE TEMPERATURE SENSE.

The sense of temperature is a very unreliable index of the actual emperature of any substance because the cutaneous surfaces yield us only relative ideas. We can say whether or not a substance is warmer or cooler than the skin, but we cannot say how many degrees of temperature it has. Knowing the probable temperature of the skin one can, by practice, usually guess approximately what the temperature of an object is; but at best the determination is based upon a eries of judgments, all of them subject to considerable error.

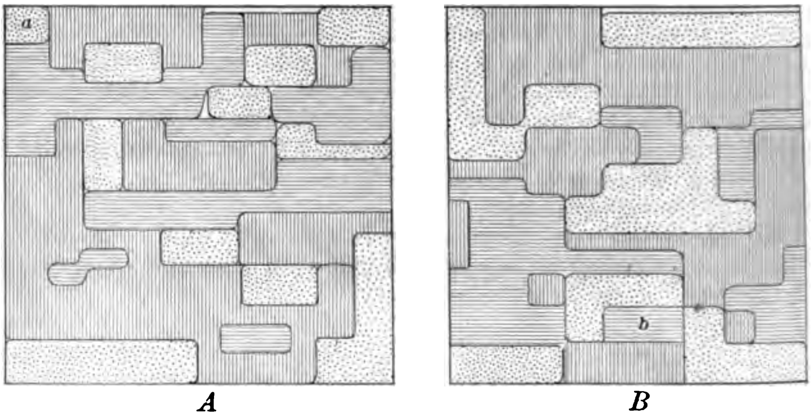
Not all portions of the surface of the skin are able to yield temperature sensations, and not all portions so endowed yield sensations of both heat and cold. One small area responds to cold, one to heat, and another to neither. The areas which do not respond to heat or old are usually endowed with the tactile sense. Nearly all portions of the skin are sensitive to pressure stimuli; but most persons seem to be more sensitive to very light pressure stimuli upon the tactile areas han upon the temperature areas (hot and cold spots); this may be an illusion due to the partial distraction of the attention by the sensation of cold or heat when an object touches a temperature area, while there is no such distraction when the object touches a tactile area.

The accompanying maps show the distribution of these areas on particular surfaces, and give a general idea of the relative sizes, shapes, and areas of cold, hot, and pressure spots. From these maps and many others the following conclusions have been drawn:

(1) Certain areas of the skin are functionally differentiated to receive stimuli from objects warmer than the skin and certain areas to receive stimuli from objects colder than the skin.

(2) Homologous areas on different individuals are different from each other as to distribution of the cold and heat areas.

FIG. 217



Two maps showing areas of temperature sense. The maps each represent an area of one square inch on the back of the left hand of Mr. A. and of Mr B. The axis of the limb is from right to left, or horizontal, as the figure stands. The "hot" spots are shaded horizontally; the "cold" spots vertically. The areas especially endowed with tactile sense are dotted. The tactile spot *a* measures $^1/_{100}$ square inch; the "hot" spot *b* measures $^2/_{100}$ square inch.

(3) The total area sensitive to cold is much greater than the total area sensitive to heat. If a piece of cold metal one inch square were laid upon the surface mapped from Mr. A.'s hand it would stimulate 49.5 cold areas and 27 pressure areas, or a total of 76.5 areas. If a piece of warm metal be applied to the same area it would stimulate 23.5 heat areas and 27 pressure areas = 50.5. This may account for the illusion that when two pieces having the same weight, one being cold and the other warm, are laid upon contiguous areas the cold one will seem to be heavier than the warm one.

(4) As a rule the longitudinal axis of an area corresponds to the longitudinal axis of the part (arm or leg) examined.

(5) Symmetrically located areas on the same individual vary considerably in their distribution of heat, cold, and pressure sensibility.

(6) Special areas—*i. e.*, heat areas or cold areas—are smaller n individuals showing greater sensibility in the æsthesiometer xperiments.

(7) Certain small areas seem to be sensitive to neither pressure, eat, nor cold when the stimuli are moderate.

(8) A test point, though varying only slightly in temperature, ay at one location feel cool, on another cold, and on a third very old.

(9) On the palm of the hand the points specialized in sensibility heat or cold are smaller and fewer than in the same area on the ack of the hand.

(10) A cold penny placed on the palm of the hand feels much naller than when placed on the back of the hand.

B. THE SPECIAL SENSES.

An organ of special sense involves: (I) a sensory end organ limited location and specialized in structure; (II) an afferent conducting ath which differs in no way histologically from other axis cylinders, ough it is a dendrite of the neurone, histogenetically; (III) a brain entre which is a portion of the general sensorium; (IV) intercentral onducting paths between the sensorium and higher cerebral centres.

An act of special sensation involves: (I) special *stimulation* of the nd organ; (II) *transmission* to the sensorium; (III) *sensation*, or onsciousness of the stimulation; these steps usually lead to the ollowing: (IV) *perception* of the stimulating object; (V) *conception* of e object in its relation to other objects.

The *special sensations* include seeing, hearing, smelling, tasting, r vision, audition, olfaction, and the gustatory sense.

The researches of Kupffer[1] and Froriep[2] show the origin of the rgans of special sense from primitive structures in the lower verte-rates.

Fig. 218 is a reproduction of Kupffer's figure of the branchial sense rgans of the larval cyclostome—Petromyzon. Note in the figure e five cephalic ganglia: I, ciliary ganglion; II, trigeminus; III, custicofacial; IV, glossopharyngeal; V, vagus, which is continuous ith the lateral nerve. Note the chain of epibranchial ganglia from to 12; the anterior four being much crowded together, the last eight eing evidently segmental, the 5th, 6th, and 7th corresponding efinitely with the III, IV, and V cephalic ganglia, respectively. Note lso the brain (*B*), spinal cord (*Sp. Cd.*), lens of the eye (*l*), the asal pit (*n*), the hypophysis or preoral pit (*Hy*), mouth (*M*), the ill clefts (*Cl*), the otocyst (*Ot*), and the notocord (*N. C.*).

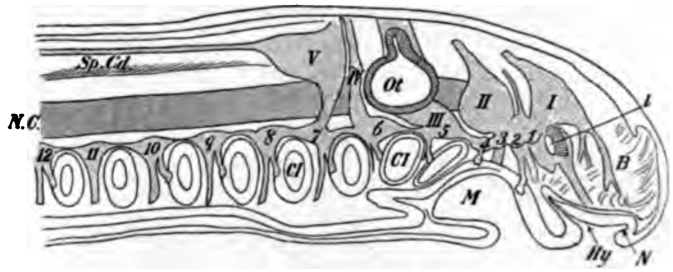
---

[1] Cephalic Nerves, Verh. Anat. Ges., München, v. 22.

[2] Sense Organs, Arch. f. Anatomie, 1886.

Kupffer says, regarding the development of sense organs: "There can be little doubt that the lateral ganglia (cephalic ganglia) and their sense organs as one series and the epibranchial ganglia and their sense organs as another series *are common to all vertebrates.* It seems *certain* that the ear, *probable* that the olfactory organ, and *possible* that the eye all belong to the lateral series."

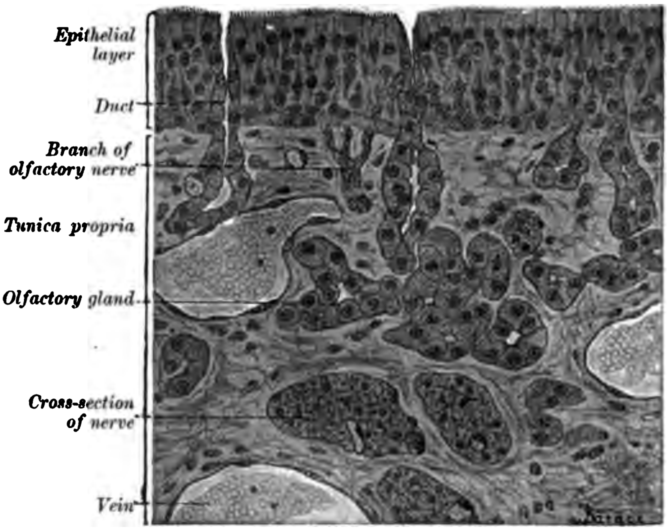
FIG. 218



Larval Petromyzon, showing branchial sensory ganglia. (Edinger, after Kupffer.)

Froriep discovered a series of rudimentary sense organs associated with the epibranchial ganglia. They are now generally known as branchial sense organs. Minot (1892) believed it probable that further investigation would "*demonstrate the existence of both series in the embryos of all vertebrates.*" Edinger (1896) cited recent literature showing that the probability has become practically a certainty.

FIG. 219



Section of olfactory mucous membrane.

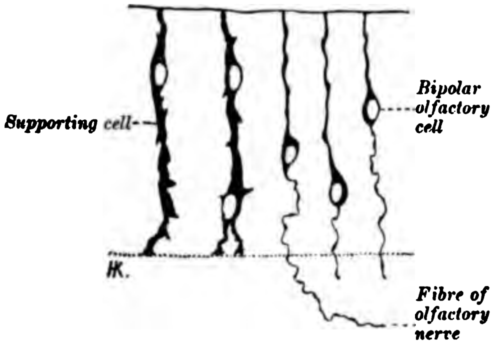
We are, then, justified in looking upon the mammalian ear as a highly specialized product of evolution of one pair of a long series of lateral sense organs. In the higher vertebrates the other lateral sense organs are either specialized in other directions (eye, olfactory organ), are rudimentary in the adult, are rudimentary and transitory in the embryo, or, finally, wholly wanting even in the embryo.

IV. THE SENSE OF SMELL.

a. Structure of the Olfactory Organs.

The end organ of smell may be described as the *regio olfactoria*, or upper part of the nasal passage, embracing the whole surface of the upper with the upper part of the middle turbinated bone, also the upper one-third of the nasal septum. This region is out of the direct line of respiration, and all of the lower region or all of the nasal passage not included in the above enumeration, is called the *regio respiratoria*. The regio olfactoria is so constructed as to present a very large surface to the air which passes through it. The mucous membrane of the olfactory region has a very thick, spongy corium, in which are located the mucus-secreting glands of Bowman, and through which pass the fibres or fibre bundles of the olfactory nerves on their way to the cribriform plate of the ethmoid bone. The epithelium consists of two kinds of cells. The epithelium proper or the supporting cells occupy most of the surface and extend to the corium by branching proximal ends. Between the supporting cells lie the olfactory cells or the *fila olfactoria*. The bodies of these cells lie deep in epithelial layer, and there is a thin, rod-like extension passing out to the surface

FIG. 220



From a vertical section through the mucous membrane of the regio olfactoria of a quite young dog. × 450. (Golgi's method.)

of the epithelium distally, while the proximal extension is really a naked axis cylinder which, joining several of its fellows, passes as a non-medullate nerve into the olfactory bulb, which lies above the cribriform plate. The interesting morphologic feature shown here is in the homology between the olfactory cells and the cells of the spinal ganglia. The distal, protoplasmic extension of the olfactory cell is the afferent cell branch or the *dendrite*, while the proximal, protoplasmic extension is the efferent cell branch or the neuraxone, here modified into a naked axis cylinder. This cell is a neurone of the I order.

FIG. 221

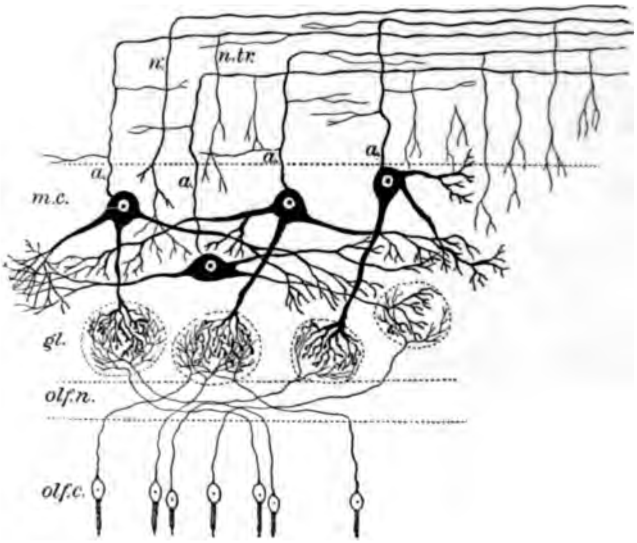


Diagram to show the relations of cells and fibres in the olfactory bulb: *olf.c.*, olfactory cells of M. Schultze in the olfactory mucous membrane, sending their basal processes as non-medullated nerve fibres into the deepest layer of the olfactory bulb (*olf.n.*); *gl.*, olfactory glomeruli containing the terminal arborizations of the olfactory fibres and of processes from the mitral cells; *m*, mitral cells, sending processes down to the olfactory glomeruli, others laterally to end in free ramification in the nerve-cell layer, and their axis-cylinder processes, *a*, *a*, upward, to turn sharply backward and become fibres of the olfactory tract (*tr. olf.*). Numerous collaterals are seen curving off from these fibres; *n'*, a nerve fibre of the olfactory tract, apparently ending in a free ramification in the olfactory bulb. (Schafer.)

This neuraxone undergoes arborization in the olfactory glomeruli, where they are in communication with the dendrites of the mitral cells of the olfactory bulb. (See Fig. 221.)

b. Physiology of the Sense of Smell.

Olfactory sensation may be stimulated by gaseous or volatile substances; the requisite conditions seem to be that the matter shall be finely divided and diffused through the air. The act of inhalation carries a direct current of the odor-laden air along the regio respiratoria, but it diffuses readily into the regio olfactoria. To aid this diffusion most mammals intuitively "sniff" when they wish to "scent" an object. The sniffing consists in a series of quick inspirations. The rarefaction of the air in the olfactory region incident to the sniffing facilitates rapid diffusion of the odor-laden air into that region.

The stimulation of the olfactory cells by the odoriferous substance can take place only through *direct contact* of the substance with the cells. To this end the substance passes into solution in the film of moisture which covers the epithelial surface. The stimulating substance is in solution when the stimulation takes place. The sense of smell is much impaired or even suspended if the olfactory epithelium should become dry from any cause. On the other hand, odoriferous substances in solution in water do not stimulate the sense of smell when the water fills the nose. The water impairs the sensibility of the olfactory cells. But if an odoriferous substance in solution in normal saline solution be brought into contact with the olfactory epithelium the olfactory cells respond to the stimulus.

The *intensity* of the sensation varies with (I) the area of the olfactory surface; (II) the concentration of the odoriferous substance; and (III) the frequency of conduction of the vapor to the olfactory region (the frequency of the "sniffs"). (Landois.)

The *acuteness* of the sense of smell varies with (I) the size of the olfactory area, and (II) practice.

All attempts at a satisfactory *classification of odors* have failed.

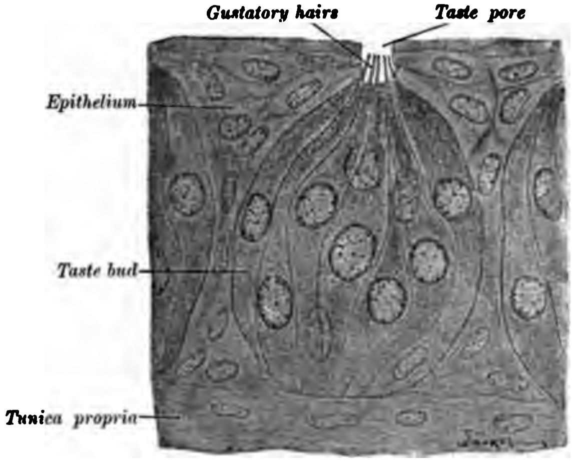
The *use of the sense of smell* to the system is primarily as a means of protection, warning the animal against the introduction of noxious foods, air, or drinks into the system, also to use in the choice of foods and drinks. Secondarily, it is cultivated by some as a means of sense gratification—witness the use of perfumes.

V. THE SENSE OF TASTE.

a. Structure of the Gustatory Organs.

The tongue serves the function under consideration, but that organ serves also other functions—*e. g.*, mastication, deglutition, and articulation of speech. The tongue is not the specialized end organ of taste. The specialized organ is the *taste bud* (Fig. 222). Numerous taste buds may be found in the epithelium of the oral mucous membrane. The figure shows that the taste bud is an epithelial structure—*i. e.*, that it is a group of modified epithelial cells. The pavement epithelium of the oral mucous membrane is not adapted to the ready absorption of liquid. The bundle of

FIG. 222



A taste bud. (Szymonowicz.)

FIG. 223

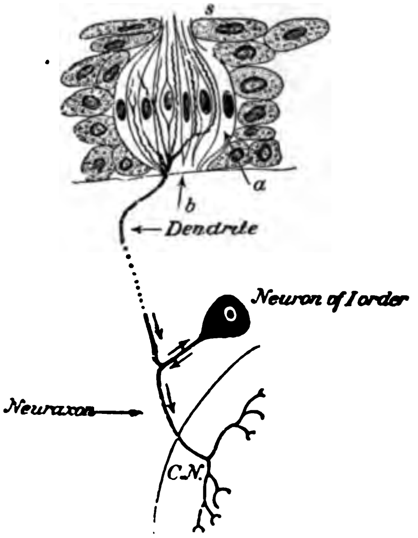


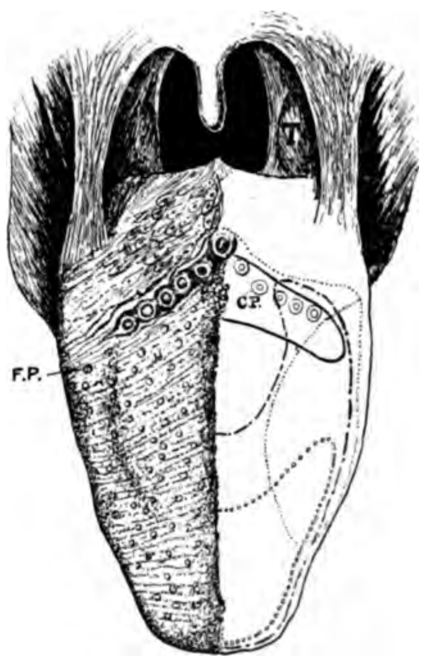
Diagram of taste bud with gustatory nerve. Note that the epithelial cells which compose the taste bud are broad encasing cells, (*a*) or slender gustatory cells. (*b*) Note the afferent dendrite arborizing among the gustatory cells and the efferent neuraxone passing into the central nervous system (*C. N.*), where it comes into relation with neurones of the II. order. The cell body is located in the trunk ganglion of the nerve of taste. (Quain, after Retzius.)

spindle-shaped cells presenting their ends at the surface of the general epithelium is well adapted to the ready absorption of liquid, and this absorption of liquid seems to be an important part of the special function of the taste buds. The accompanying diagram (Fig. 223) makes it evident that liquid absorbed from the surface (*s*) of the epithelium will pass, by capillary attraction, between the spindle-shaped gustatory cells and be brought into intimate contact with the filamentous ends of the gustatory nerve.

If the liquid be an aqueous solution of some substance capable of stimulating the sensation of taste, the effect of the stimulation will be propagated along the afferent dendrite to the cell body of the neurone which lies in the ganglion of the nerve trunk, thence through the neuraxone to the central nervous system, within which a neurone of the second order transmits it to the sensorium. There has been much controversy as to whether the gustatory nerve fibres are all contained in the glossopharyngeal trunk, or whether some of them may not reach the oral mucous membrane through the lingual branch of the trigeminus. Both nerves undoubtedly contain gustatory fibres. The gustatory fibres may readily pass from one trunk to another in the tympanic plexus, a condition which is known to exist in the case of the secretory and vasodilator fibres of the salivary glands (*q. v.*). There is probably one source for the gustatory nerve fibres, and that source is probably the trunk (petrous) ganglion of the glossopharyngeal nerve.

The taste buds are distributed (I) over the lateral surfaces of the circumvallate papillæ; (II) upon the fungiform papillæ; (III) upon the papillæ of soft palate, uvula, anterior pillars of the fauces, and surface of epiglottis.

FIG. 224



Map of tongue, showing papillæ on the left and localization areas on the right: *T*, tonsil; *F.P.*, fungiform papillæ; *C. P.*, circumvallate papillæ. Area sensitive to bitter (———); acid (.........); salt (—.—.—); sweet (— — ---).

b. Physiology of the Sense of Taste.

(*a*) A Summary of the Facts Concerning Taste.—Many of the perceptions attributed to taste really depend quite as much upon smell as upon taste. We usually apply the term *flavor* to those sensations which depend upon both smell and taste—*e. g.*, one speaks of the flavor of roast beef or of coffee. The fact that closure of the nose impairs the flavor of the beef or coffee indicates that a part of the flavor is to be attributed to the sense of smell. The sense of taste alone seems to be confined to sensation arising from four distinct stimuli: (I) *sweet;* (II) *bitter;* (III) *acid;* (IV) *salt.* All taste sensations are either modifications of or combinations of these four fundamental sensations.

The sense of taste is usually excited by those substances which pass into solution—*i. e.*, insoluble substances are tasteless. Though this applies to the chemical substances alone, it must not be forgotten that these are incomparably the most important stimuli of the sense of taste. In the case of electric stimuli the fact that the cathode usually tastes bitter-alkaline while the anode tastes acid would seem to show that the efficient stimulus in either case is the collection of bases and acids which gather at the two poles respectively. Though this is undoubtedly the way to account for the taste of the anode and cathode in the case of the constant current, it does not throw much light upon the fact that taste sensations are also aroused by induction shocks.

The sensation will vary in strength with (I) the *size of the area stimulated,* being more intense the greater the area stimulated; (II) the *concentration of the solution,* being more intense the stronger the solution; (III) the *temperature of the solution,* being more intense the nearer the temperature is to that of the blood; (IV) the mechanical friction of the tongue against the palate, being stronger with moderate friction than without it.

The sense of taste varies in acuteness (I) through certain hereditary influences and (II) through cultivation. A good example of marked acuteness of taste acquired by cultivation may be found in the professional tea-tasters and wine-tasters.

(*b*) **Localization of the Sense of Taste.**—If solutions of salt, of sugar or saccharine, of quinine, and of acetic, malic, or citric acid be applied to the tongue with a probang it will be found that not all parts of the tongue are equally sensitive to these several stimuli. The back of the tongue is more sensitive to bitter, the sides to acid, the dorsum to salt, and the tip to sweets. Fig. 224 shows the outline of these areas.

(*c*) **The Acuteness of the Sense of Taste.**—If standard solutions of salt, sugar, quinine, and acetic acid be made, the acuteness of the sense of taste for these substances may be determined in individual cases. The average limit of acuteness as determined for a large number of individuals is: (I) for salt 1 part to 469 of distilled water; (II) for sugar, 1 to 520; (III) for acetic acid, 1 to 5640; (IV) for sulphate of quinine, 1 to 375,000.

VI. HEARING.

INTRODUCTORY.

1. Physiologic Acoustics.
2. Comparative Anatomy and Physiology of the Auditory Organ.
3. Embryology of the Auditory Organ in Vertebrates.
4. Summary of the Anatomy and Histology of the Ear.

THE PHYSIOLOGY OF HEARING.

1. The Transmission of Sound.
    - (a) *The Part Played by the External Ear.*
    - (b) *The Part Played by the Middle Ear.*
2. The Reception of Sound.
3. The Sensation and Perception of Sound.

1. PHYSIOLOGIC ACOUSTICS.

a. Definitions.

(*α*) Acoustics is the Science of Sound, and comprises the study of sounds and of the vibrations of elastic bodies. Acoustics is concerned particularly with questions of the production, transmission, and comparison of sounds.

(*β*) "Sound is always the result of rapid oscillations imparted to the molecules of elastic bodies, when the state of equilibrium of these bodies has been disturbed either by a shock or by friction." (Ganot.) Such bodies, always representing ponderable matter, tend to regain their position or condition of equilibrium only after performing on each side of that position very rapid vibratory movements the amplitude of which quickly decreases. The term *sound* is also applied to the sensation which these vibrations arouse in the brain.

(*γ*) The term Physiologic Acoustics may be applied to that portion of the general field of acoustics which deals with the production, transmission, and comparison of the sounds made by animals, or of the sounds serving as stimuli for animal sense organs. Physiologic acoustics deals, then, with the physical principles involved in the production of the voice; with speech, music, and the transmission of these sounds by the organs of hearing to the auditory nerve ends.

b. The Production and Propagation of Sound.

Sound is produced by the vibration of elastic bodies. A musical sound or tone is a regular continuous sound. *A noise* is an irregular discontinuous sound.

Sound can be propagated only through the medium of ponderable matter, for if the air be withdrawn from the receiver of an air-pump a music-box in operation within the receiver, surrounded by the imponderable, luminiferous ether, cannot be heard.

Sound is propagated through elastic, ponderable matter. All gases, liquids, and solids may transmit sounds. These bodies are acted upon by the vibrating source of the sound and are thrown into a series of waves which rapidly spread in all directions from the centre of disturbance. In water-waves, or the undulations which sweep over the surface of a body of water, the individual molecules rise and fall, describing an ellipse whose long axis is *transverse* to the direction of propagation. In sound waves the molecules move to and fro in a line *parallel* to the direction of propagation. This leads to *a series of alternating condensations and rarefactions of the medium.*

1. **Velocity of Propagation of Sound.**—A general formula for velocity is

$$v = \sqrt{\frac{\varepsilon\gamma}{\delta}},$$

when ε represents the elasticity, γ the specific heat, and δ the density.

(*a*) **In Gases.**—Newton determined that the velocity of the propagation of sound in gases *is directly as the square root of the elasticity of the gas, and inversely as the square root of its density.* This formula with modifications for temperature and barometric pressure yields the following results: velocity of sound in carbon dioxide, 856 ft. per sec.; oxygen, 1040 ft.; air, 1093 ft.; hydrogen, 4063.

(*b*) **In Liquids.**—The general formula

$$\left(v = \sqrt{\frac{\varepsilon\gamma}{\delta}}\right)$$

may be applied with modifications for liquids. The coefficient of elasticity (ε) is very high for liquids, and though the density (δ) is also great the high elasticity makes the velocity of sound in liquids much higher than it is in gases. For water the velocity is 4708 ft. at 80° C. to 5013 ft. per sec. at 30° C.; for absolute alcohol, 3854 ft. per sec. at 23° C.; for a solution of NaCl, 5132 ft. per sec. at 18° C.

(*c*) **In Solids.**—The velocity in feet per second in caoutchouc, 197 ft.; in lead, 4030 ft.; in copper, 11,666 ft.; in steel wire, 15,470 ft.

2. **Reflection and Refraction of Sound.**—The echo, familiar to every youth, is a simple reflection of sound. The reflection of sound is subject to the following laws: (I) *The angle of reflection of sound is equal to the angle of incidence.* (II) *The incident sonorous ray and the reflected ray are in the same plane perpendicular to the reflecting surface.*

A *sound lens* made of two circular sheets of collodion cemented together at their edges and inflated with CO_2 will bring sound waves to a focus. The ticking of a watch held beyond the principal focus of such a lens may be clearly heard in the conjugate focus of the lens, though the conjugate focal distance may be many feet.

c. The Properties of Sound.

One sound may vary from another in intensity or loudness, in pitch, and in quality.

1. **Intensity.**—(I) The intensity of sound varies inversely as the square of the distance of the sonorous body from the ear.

$$\left(I \text{ varies as } \frac{1}{D^2}\right).$$

(II) The intensity of sound increases with the amplitude of the ibrations of the sonorous body.

(III) The intensity of sound depends on the density of the air hrough which the sound is propagated.

(IV) The intensity of sound is modified by the motion of the tmosphere by the wind.

(V) The intensity of sound is increased by the proximity of a onorous body—*e. g.*, the sounding box of a violin intensifies the ound produced by the vibration of the strings.

2. **Pitch.**—The expression "pitch of a sound" refers to the number of vibrations of the sonorous body in a unit of time. The greater he number of vibrations per second, the *higher* the pitch; the fewer he vibrations, the *lower* the pitch. The number of vibrations which a sonorous body will make in a second depends upon several variable actors. In physiologic acoustics we are interested particularly in he vibrations of strings and of membranes, because the human voice s the sound of the vibrating strings—*the vocal cords;* and the hearing of the human voice and other sounds depends upon the vibration of a stretched membrane—*the membrana tympani.*

(*a*) **The Pitch of a Vibrating String.**—Rayleigh (*Sound*, Vol. I., Chap. I.) gives the following formula for a vibrating string:

$$\text{(I)}\quad n = \frac{1}{2rl}\sqrt{\frac{981g}{\pi\delta}}.$$

Equation (I) expresses the number of vibrations per second in terms of length (l), radius (r), tension (g), and density (δ). Expressed as a variable by dropping the constants:

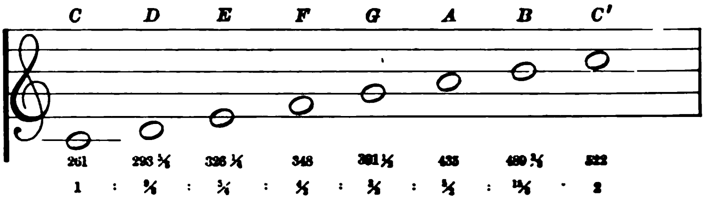
$$\text{(II)}\quad n \text{ varies as } \frac{1}{rl}\sqrt{\frac{g}{\delta}}.$$

The verbal expression of the formula is: *The vibration frequency* (pitch) *of a string varies* (I) *inversely as the radius;* (II) *inversely as* *the length;* (III) *directly as the square root of the tension in grams;* (IV) *inversely as the square-root of the density.*

(*b*) **The Pitch of a Vibrating Membrane** may be determined by the above formula (II) under certain conditions: (I) the membrane must be circular (*l*), like a drum head; (II) the tension (*g*) must be equal in all directions in the plane of the circle; (III) the thickness must be equal in all parts (*r*); (IV) the density must be equal in all parts. Once these conditions are filled we have in a vibrating membrane the equivalent of an infinite number of strings of equal length, tension, radius, and density, which will, of course, vibrate in unison —*i. e.*, the membrane will give the same fundamental tone as that given by a string representing a diameter of the membrane.

(*c*) **The Musical Scale.**—The standard pitch of an instrument is *A* which represents 435 vibrations per second; it is the middle *A* of the pianoforte. Note that the tone *C′* has just twice the number of vibrations of *C*. This relation holds good throughout the whole musical scale: *A′* has (435 × 2 =) 870 vibrations per second; while A_1 (one octave below middle *A*) has ($\frac{435}{2}$ =) 217½ vibrations per second. The lowest *C* (C_3) of the piano has 32 + vibrations per second and the lowest *C* (C_4) of the pipe organ has 16 + vibrations per second; middle *C* (*C*) has 261 vibrations per second; C^{I} has 522; C^{II} has 1044 vibrations per second; C^{III}, 2088; C^{IV}, 4176; C^{V}, 8352; C^{VI}, 16,704; C^{VII}, 33,408, etc. The number of vibrations of any note may be determined by multiplying the number for the next *C* below the note in question by the ratio indicated in the accompanying figure.

FIG. 225



3. **Quality.**—The variation in quality depends upon the combination of *harmonics*, or *overtones*. The degree of complexity of a sound—the number of overtones present—together with the relative prominence or loudness of each overtone, is interpreted mentally as giving a distinctive *quality*, or *timbre*, or character to the sound heard. When one hears the *A* of a violin he not only recognizes the pitch and intensity, but he is able to say that it is produced by the violin. One does not consciously hear the harmonics, or overtones, as a rule; he hears only the fundamental tone *of a certain quality*. The flute gives practically a pure fundamental tone without any overtones.

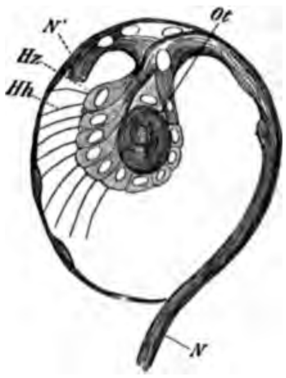
With a series of flutes which produce notes whose frequencies are in the ratios 1 : 2 : 3 : 4 : 5, so mounted in a wind apparatus that they may be made to sound with a loudness which can be separately regulated, one can *build up any quality of sound.* Thus the infinite variety of sounds one hears in nature is very simply explained. Even the different vowel sounds depend for their differences upon the *modification in quality of a fundamental laryngeal tone*—given a particular quality by resonance of the organs of articulation—pharyngeal, oral, and nasal cavities.[1]

2. COMPARATIVE ANATOMY AND PHYSIOLOGY OF THE AUDITORY ORGANS.

There is no reason to believe that any of the Protozoa are sensitive to atmospheric vibrations. If they respond to the audible vibrations of the liquid media in which they rest, it is probable that these vibrations are really mechanical stimuli for their light unicellular bodies.

Some Cœlenterata possess auditory vesicles lined with epithelial cells, provided with bristle-like cilia, an otolith, and innervated by a nerve. Fig. 226 shows a section through such a simple auditory organ.

FIG. 226



Auditory vesicle of a jelly-fish enclosing fluid provided with one or more otoliths: *N*, nerve; *Ot*, otolith; *Hz*, auditory cells with hairs, *Hh*. (Mills, after Claus.)

Among the *Echinodermata* only deep-sea holothurians, *Elasipoda*, possess auditory vesicles (56 in number). These are located along the course of the nerve cords and possess numerous otoliths.

The *Vermes*, as represented by the common earthworm, *Lumbricus*, though externally sensitive to the vibrations of the solids upon which they rest, are quite insensible to vibrations of the air. The microscope reveals no auditory vesicle in the earthworm.

The auditory vesicles of the *mollusca* are constructed upon the same general plan as those of the medusa. Fig. 227 shows Claus' section of the auditory vesicle of a heteropod mollusk. In most Lamellibranchs and Gasteropods and in the nautilus the auditory vesicles are innervated from the pedal ganglia.

The *Arthropoda* have more highly developed external ears than can be found elsewhere among the invertebrates. The crustacea as represented by the crayfish has auditory organs at the base of the antennules. "Here the auditory sac is permanently open,

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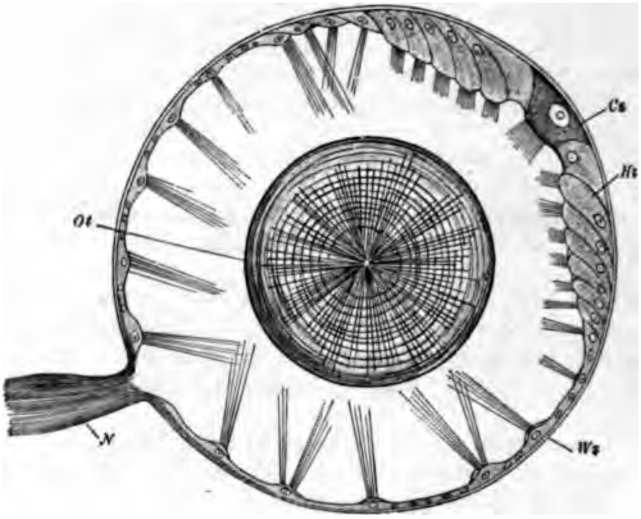
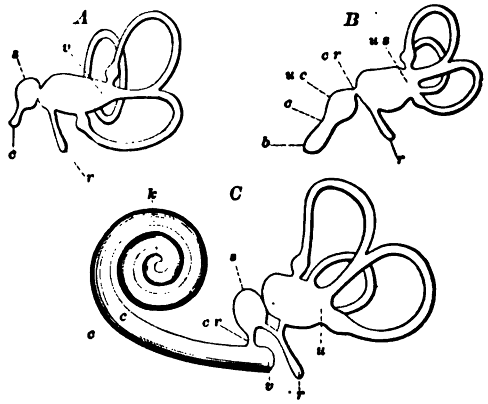
[1] Daniell. Medical Physics.

FIG. 227



Auditory vesicle of a heteropod mollusk (Pterotrachea): *N*, auditory nerve; *Ot*, otolith in fluid of vesicle; *Wz*, ciliated cells on inner wall of vesicle; *Hz*, auditory cells; *Cz*, central cells. (Mills, after Claus.)

FIG. 228



Diagrams to show the relations of the auditory labyrinth in the vertebrate series: *A*, fish; *B*, bird; *C*, mammal; *u*, utriculus, with the three semicircular canals; *s*, sacculus; *c*, cochlea; *r*, aquæductus vestibuli; *b*, lagena; *c r*, canalis reuniens. In *C*, *r* is seen to divide into separate passages for the utriculus and sacculus; the vestibule is seen to have a cæcal sac at *r*; *k*, coil of the cochlea. (After Waldeyer.)

though protected by bristle-like setæ. Within this sac a part of the wall is raised up into a ridge, and the cells that form it are pro-ith delicate setæ at their free end and with nerve fibres base within. The sac is filled with a gelatinous fluid con-minute otoliths. Vibrations of the external medium set iths in motion; these beat upon the setæ, and these setæ e cells on the acoustic ridges, which, in turn, stimulate the bres which are in direct communication with the brain."

The grasshopper, representing the *Insecta*, has a tympanum. a modification of the chitinous integument and consists of a cross which a delicate chitin membrane is stretched, held taut licate rim which in turn is stretched by a number of small uscles. Within the tympanum is an auditory ridge homol- that described above in the crayfish.

ertebrata show the ear in its highest development.

gher vertebrates possess an internal ear (modified auditory of considerable complexity, showing a *vestibule* and a series *ircular canals.* The mammals possess in addition a complex called the *cochlea.* Waldeyer's figure (Fig. 228) shows the is in the structure of the auditory vesicle in fishes, birds, mmals.

RYOLOGY OF THE AUDITORY ORGAN IN VERTEBRATES.

a. Comparative Embryology.

rigin of the ear from one of the lateral ganglia of the petro-as maintained by Kupffer and now generally accepted, has cussed above. (See p. 568.)

owest mammals show a clear relation to the birds in the eps of development, a relation which is not by any means in the adult structure.

b. Special Embryology of the Human Ear.

velopment of the External Ear.—The external meatus nds to the invaginated part of the branchial cleft and is, e, lined with epiblast. The pinna is developed (Fig. 229) eminences which surround the external end of the meatus. fourteenth week the form has already approximated that of lt ear.

imes the pinna is arrested in its development. The small, hick ear, such as shown in *D*, is almost sure to be associated reater or less degree of arrest of psychic development.

velopment of the Middle Ear.—For the details of the de-nt of the middle ear, especially the bones of the middle ear, see any work on the histogenesis of the pharynx. The following is a summary:

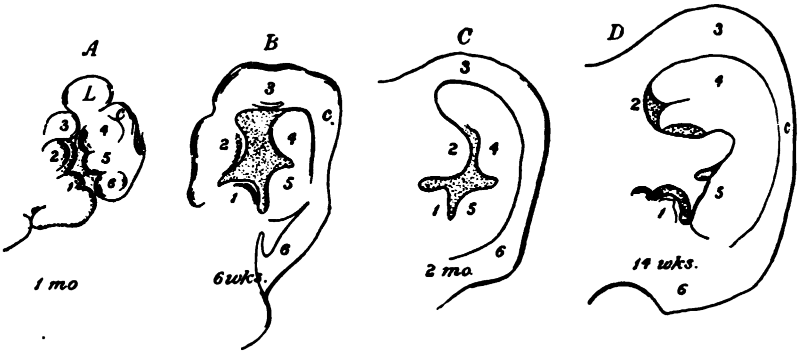
(I) The tympanic cavity and the Eustachian tube are developed from the first branchial pouch, hence called the "*tubotympanal pouch.*" It is lined with hypoblast.

(II) The malleus is developed from a part, probably the ceratobranchial segment, of the 1*st branchial arch.*

(III) The incus is developed from a part, probably epibranchial segment, of the 1*st branchial arch.*

(IV) The stapes is developed as an osseous deposit in the ligamentous connective tissue, connecting the fenestra ovalis with the incus. The hole in the stapes, which gives it its distinctive form, was occasioned originally by the presence of an artery, around which the ossification took place.

FIG. 229



Development of the pinna: 1, tragus; 2, 3, *C*, helix; 4, anthelix; 5, antitragus; 6, tænli lobaris. (Minot.)

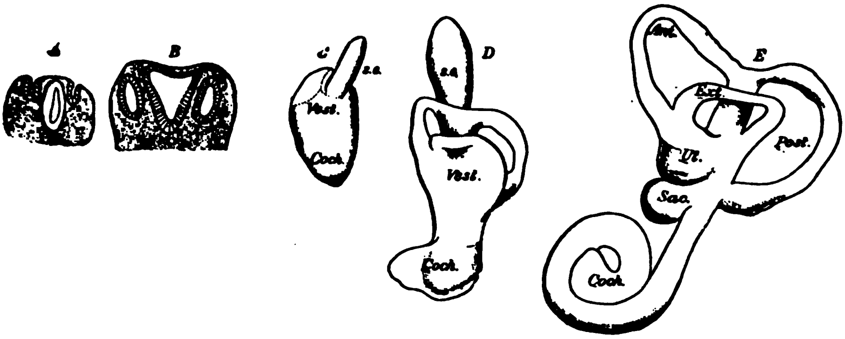
3. **The Development of the Labyrinth.**—*The Otocyst:* In the earliest stages of embryonic development, when the anterior end of the neural tube has been definitely divided into primary forebrain, midbrain, and hindbrain vesicles, there appears on either side of the hindbrain vesicle a minute pit, which is invaginated from the epiblast and therefore lined with epiblast. This pit, the beginning otocyst, continues its invagination until it divides off from epiblast and begins a gradual migration through the delicate mesenchymal embryonic tissue toward its future position (Fig. 230, *A* and *B*.)

In the mean time the otocyst rapidly enlarges and by the fourth week the saccus endolymphaticus (*s. e.*) is beginning its development (Fig. 230, *C*).

The third stage marks the development of the semicircular canals (Fig. 230, *D* and *E*). Note the order in which these are developed. Note also the development of the cochlea.

From this series of figures it is evident that the epithelial lining of the membranous labyrinth is epiblastic. At first composed of undifferentiated columnar cells there comes to be, in man, six areas within the membranous labyrinth where the epithelium is highly differentiated. Of these the most highly specialized is the organ of Corti, which undoubtedly represents the end organ for the perception of sound. Besides the organ of Corti there is one specialized area in each semicircular canal—the *crista acustica,* and one in the utriculus, the *macula acustica utriculi.*

Fig. 230



Development of the membranous labyrinth. Beginning of otocyst in the human embryo: *A*, 2.4 mm. in length; *B*, 4 mm. in length; *C*, otocyst of human embryo, four weeks (His); *D*, human embryo, five weeks (His); *E*, membranous labyrinth of two months' embryo (His). (Minot.)

4. SUMMARY OF THE ANATOMY AND HISTOLOGY OF THE EAR.

(1) The organ of hearing is divisible into (I) external, (II) middle, and (III) internal ear; or (I) pinna and meatus, (II) tympanum, and (III) labyrinth. (See Fig. 231.)

(2) The *tympanum* lies in a hollow in the petrous portion of the temporal bone. The tympanic membrane (*T*) cuts it off from direct connection with the external atmosphere. The Eustachian tube (*TE*) brings it into indirect connection with the air through the pharynx and external respiratory passages. The tympanum contains a chain of bones: the malleus (*h*), the incus (*a*), and the stapes (*s*). The malleus is fastened to the membrana tympani and the stapes to the membrane which closes the foramen ovalis.

(3) The *labyrinth* lies within a cavity in the petrous portion of the temporal bone. The cavity with its various canals is called the *bony labyrinth.*

(4) Within the cavity of the bony labyrinth, but very much smaller than the cavity, lies the *membranous labyrinth* (Fig. 232 *C.c.*). From the embryology it is evident that the epithelium of this membranous

labyrinth is epiblastic. Between this structure and the bony wall there is a considerable space occupied by two large lymph channels. The one above the epiblastic membranous labyrinth is the *scala vestibuli*, so-called because it is continuous with the vestibule. The one below is called the *scala tympani*, which passes to the foramen rotundum, closed by a thin but dense and strong membrane.

FIG. 231

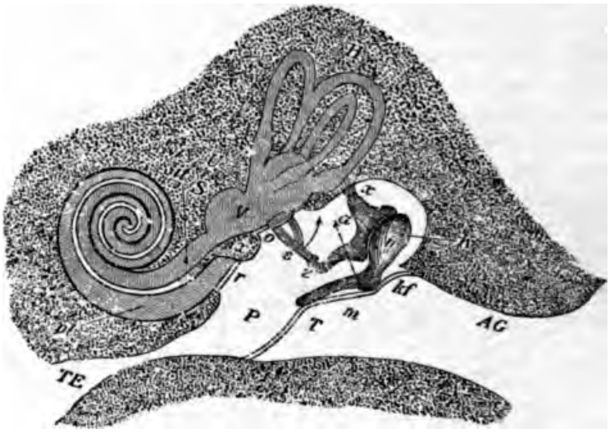
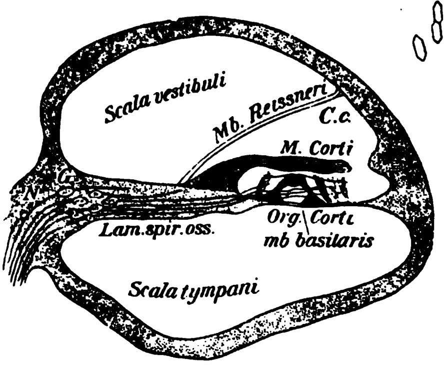


Diagram intended to illustrate the process of hearing: *AG*, external auditory meatus; *T*, tympanitic membrane; *K*, malleus; *a*, incus; *P*, middle ear; *o*, fenestra ovalis; *r*, fenestra rotunda; *pl*, scala tympani; *vt*, scala vestibuli; *V*, vestibule; *S*, saccule; *U*, utricle; *H*, semicircular canals; *TE*, Eustachian tube. Long arrow indicates line of traction of tensor tympani: short curved one, that of stapedius. (After Landois.)

FIG. 232



Cross-section of one whorl of the cochlea, with the membranous labyrinth, marked *C.c.* (Canalis cochlearis), and the large lymph spaces above and below.

(5) Note the little bony shelf (*Lamina spiralis*) which extends out from the inner wall of the bony canal and reaches about three-fifths of the way across to the outer wall, where there is a corresponding ridge. The space between the spiral lamina and the outer ridge is spanned by a dense membrane (*membrana basilaris*) which is composed in its 2½ spiral turns of about 24,000 parallel, radial fibrillæ. The length of the fibrillæ which constitute the basilar membrane varies—*i. e.*, the width of the membrane varies in different parts of the cochlea:

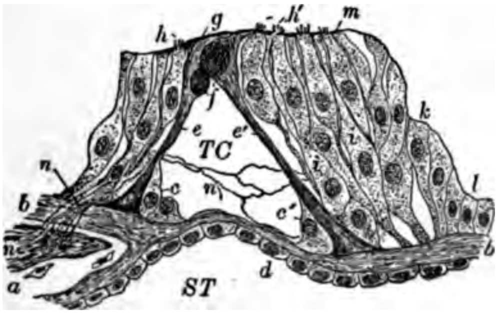
(I) At the beginning of the basal coil of the cochlea, 0.041 mm.
(II) Average for basal coil of cochlea, 0.21 mm.
(III) Average for middle coil of cochlea, 0.34 mm.
(IV) Average for apical coil, 0.36 mm.
(V) Length at end of apical turn, 0.495.

The longest fibrilla is twelve times the length of the shortest one.

(6) Between the basilar membrane and the membrane of Reissner is the epiblastic end organ of hearing—the organ of Corti.

(7) The *Organ of Corti* consists essentially of: (I) The rods or *pillars of Corti*, which are secured by the epiblastic cells *c* and *c'* (Fig. 233), and are chitinous in their general character. (II) The *inner and outer hair cells*, so-called from the short bristle-like hairs which extend from the upper ends. There are five rows of hair cells, one inner and four outer ones. (III) The supporting cells of Deiters. (IV) The reticular membrane, continuous with the outer ends of the rods of Corti and of the same sort of material as they. (V) The filamentous endings of the auditory nerve about the proximal ends of the hair cells.

FIG. 233



Section of Corti's organ from guinea-pig's cochlea. *ST*, scala tympani; *TC*, tunnel of Corti; *a*, bony tissue of spiral lamina; *b*, fibrous tissue covering same continued as substantia propria of basilar membrane; *c*, *c'*, protoplasmic envelope of Corti's pillars (*e*, *e'*); *d*, endothelial plates; *f*, beads of pillars containing oval areas; *g*, head-plates of pillars; *h*, *h'*, inner and outer hair cells; *m*, membrana reticularis; *k*, *l*, cells of Henson and of Claudius; *n*, nerve fibres; *i*, cells of Dieters. (Piersol.)

(8) There is an area of specialized innervated epithelium in the saccule and one in the utricle.

(9) The three specialized epithelial areas in the semicircular canals have been depicted and discussed under *Maintenance of Equilibrium* (q. v.).

(10) Figs. 226 and 227 show some typical otoliths.

THE PHYSIOLOGY OF HEARING.

1. THE TRANSMISSION OF SOUND.

a. Part Played by the External Ear.

1. **The Pinna, or Auricle.**—The part which it plays in man is so slight as to be practically disregarded. Abnormal projection of tragus over mouth of meatus obstructs sound waves.

2. **Meatus Externus.**—(*a*) THE CALIBRE is usually smallest at inner end near membrana tympani, though it is smaller in the middle (inner end of cartilaginous portion) than between that and the membrana tympani. If there is an abnormal narrowing of the inner segment there is no impairment of the hearing. If there is an abnormal narrowing of the outer end there is an unmistakable impairment of hearing.

(β) COURSE.—The meatus presents two segments meeting at an obtuse angle, the cartilaginous portion passes upward and inward and backward, the bony portion passing downward, forward, and inward. This makes a direct transmission impossible; the sound waves must be reflected at least twice before impinging upon the membrana tympani.

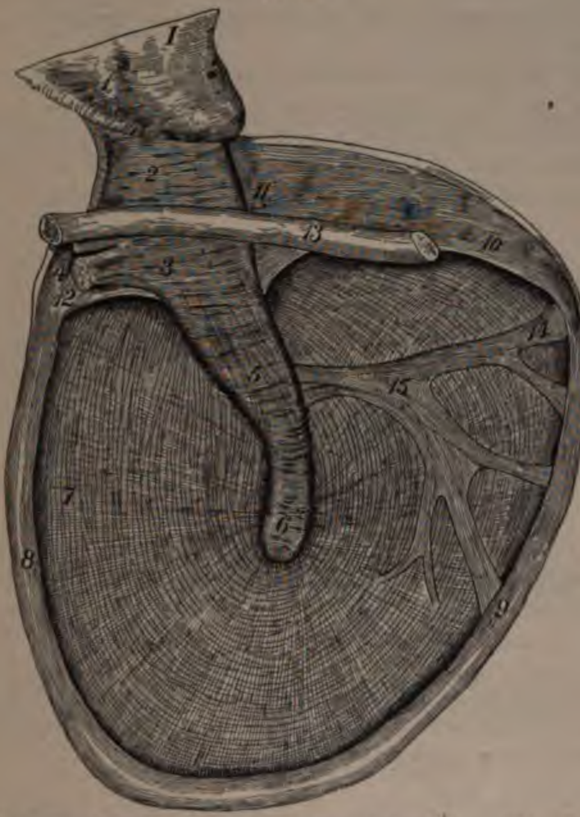
(γ) REFLECTING SURFACES.—The description already given would lead us to suppose that these surfaces are conical ones, but the cross-section of the meatus is always elliptic in general outline, and there is a depression on the *posterior* wall of the cartilaginous segment and one on the *anterior* wall of the bony segment. The more external depression presents an *ellipsoidal* surface, while the more internal one presents a *paraboloid* surface. Professor Dench in his text-book on the diseases of the ear cites this fact as advantageous.

(δ) THE HAIRS AND SECRETIONS of the meatus are for protection. They catch dust and any insects that might attempt to enter.

3. **The Membrana Tympani.**—(*a*) GENERAL STRUCTURE: This delicate membrane possesses a *skin*, a mesenchymal *framework*, and a hypoblastic *mucous membrane*. The mesenchyme consists of inelastic *connective-tissue fibres which are either circular or radial.* The accompanying figure (Fig. 234) shows the general course of the radial and circular fibres of the middle layer or framework of the membrane.

(β) The Angle at which the membrana tympani is set with respect to the axis of the bony segment of the meatus is not without importance. The lower half of the membrane inclines toward the axis of the meatus, leaving an angle of about 55 degrees and the upper half of the membrane inclines still more, leaving about 45 degrees or less between membrane and axis. (See Fig. 235.)

Fig. 234



Photographic representation of right membrana tympani viewed from within: 1, divided head of malleus; 2, neck; 3, handle, with attachment of tendon of tensor tympani; 4, divided tendon; 5, 6, long handle of malleus; 7, outer radiating and inner circular fibres of tympanic membrane; 8, fibrous ring encircling membrana tympani; 9, 14, 15, dentated fibres of Gruber; 10, 11, posterior pocket connecting with malleus; 12, anterior pocket; 13, chorda tympani nerve. (After Flint and Rüdinger.)

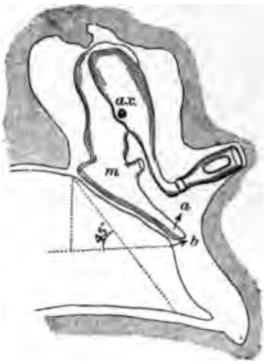
(γ) The Area of the Membrane.—It presents an elliptical surface whose axes are about 10 and 8 mm. The area would be approximately ($a = \pi r^2$; $a = 3.1416 \times (4.5)^2 =$) 63.5 sq. mm.

(δ) The Question of Fundamental Tone.—Every fixed taut string and typical drum membrane possesses a fundamental tone.

If the membrana tympani possessed a fundamental tone it would greatly impair its utility as a transmitting membrane for sounds of different pitch. The membrana tympani does not possess a fundamental tone because: (I) It is elliptical in outline. (II) Its vibrations are dampened by the attachment of the handle of the malleus. (III) The connective-tissue fibres which radiate outward from the handle of the malleus as a part of the substantia propria of the membrane are of various lengths and of slightly varying tension. *A fundamental tone for the membrana tympani is, therefore, an acoustic impossibility.*

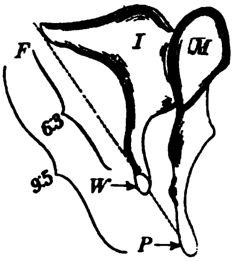
(ε) THE EXTERNAL CONVEXITY OF ITS RADIATING FIBRES.—Helmholtz has shown that an impulse against the convex surface of the taut membrane will have a greater effect in driving the handle of the malleus inward than would be the case if the taut membrane were a plane surface. When we consider, however, that the direction of this increased force would be as indicated by the arrow *a*, Fig. 235, instead of the direction of arrow *b* the required direction; the advantage is not so great as might first appear.

FIG. 235



Showing incline of membrana tympani.

FIG. 236



Lever system of the ear.

b. Part Played by the Middle Ear, or Tympanum.

(*α*) THE EUSTACHIAN TUBE permits equalization of pressure inside and outside of the cavity.

(*β*) THE LEVER SYSTEM.—For the transmission of sound the malleoincudal combination moves as one lever, while the stapes simply transmits the movements of the end of the incus to the oval window.

For protection of the membrane which closes the oval window and to which the stapes is attached, the malleoincudal articulation is subject to motion in such a direction as to permit the handle of the malleus to be displaced outward without carrying the incus with it.

The lever arms (Fig. 236) have the ratio 6.3 mm. to 9.5 mm. The maximum movement of the end of the handle of the malleus is 0.097 mm., almost 0.1 mm. The distance travelled by the weight would be $= \frac{0.097 \times 6.3}{9.5} = 0.0643$, or a little more than $\frac{1}{16}$ of a millimetre. (Helmholtz.) In the mean time the force has been augmented by the ratio $\frac{9.5}{6.3}$, or about 1.5 times—*i. e., the foot of the stapes vibrates through two-thirds the amplitude with 1½ times the force represented in the vibration of the malleus handle.*

FIG. 237

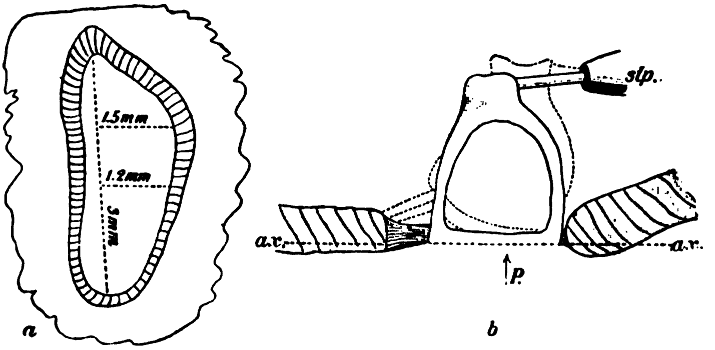


Diagram showing the shape and dimensions of the foot of the stapes (*a*) and the effect of contraction of the stapedius muscle (*stp.*) lifting the "toe" of the stapes up from the plane of the foramen (*ar.*). (After Testut.)

The size of the foot of the stapes is 2.65 sq. mm.; while the area of the fenestra = 3.8 sq. mm. The area of the annular ligament is 1.15 sq. mm.

c. The Summed-up Force.

As all of the energy received by 63.5 sq. mm. of tympanic membrane is transmitted to 2.65 sq. mm. of stapes, we have a proportionally greater intensity of vibration. The convexity of the membrane increases the intensity. Assume a ratio of 2 : 1. The lever system increases the intensity by a ratio of $\frac{9.5}{6.3}$. Summing up these ratios we have a final intensity (I) bearing the following ratio to the initial intensity (i):

$$\frac{I}{i} = \frac{63.5}{2.65} \times \frac{2}{1} \times \frac{9.5}{6.3} = 72.16$$

The intensity per unit area is multiplied many times in the course of its transmission. On the other hand, *the amplitude is decreased to only two-thirds of the original amplitude.*

d. The Movements of the Stapes.

The full-line figure indicates the position of the stapes when the stapedius muscle (*stp.*, Fig. 237) is relaxed. The dotted outline indicates the position of the stapes when the muscle is strongly contracted. This shows the motion of the stapes to be a rocking around the pivot *p*. The wider area of the annular ligament anteriorly permits the motion. The maximum amplitude of the upper end of the stapes is about 0.064 mm., or $\frac{1}{16}$ mm. That would give the anterior end of the foot an amplitude considerably more than $\frac{1}{16}$ mm. and the posterior end, or heel, an amplitude of about zero, or even possibly a slight negative vibration. But these are the conditions when the pitch is low, the amplitude of the membrana tympani great and the stapedius strongly contracted. These conditions would be likely to exist when the ear is receiving loud noises.

In the reception of the musical tones of the human voice or of a musical instrument it is not probable that the rocking motion exists. The amplitude of the motion may be as little as $\frac{1}{10000}$ mm.

e. The Perilymph of the Scala Vestibuli.

This takes up the vibrations of the foot of the stapes and transmits them to the organ of Corti, and through the scala tympani back to the foramen rotundum, whose membrane serves to equalize and temper the pressure within the labyrinth.

2. THE RECEPTION OF SOUND.

The end organ of sensation is the organ of Corti. The modified epiblastic cells are the hair cells of the organ of Corti. About these modified epiblastic cells, or special receiving cells, the dendrites of the cochlear branch of the auditory (VIII) nerve arborize. The cell body of the auditory neurone of the *I* order (whose dendrites arborize about the hair cells) lies in the spiral ganglion; the neuraxone passes to the sensorium of the central nervous system. The way in which the terminal nerve ends are stimulated is a matter of speculation.

(*a*) THE HARP THEORY OF HELMHOLTZ briefly expressed is: 1st. The vibrations of the medium received by the membrana tympani are transmitted across the tympanic cavity and to the perilymph of the vestibule, with somewhat decreased amplitude, but much increased intensity, as given in detail above. 2d. The perilymph as well as the endolymph of various canals of the cochlea take up vibrations which correspond in number per second (pitch) with their own. 3d. The hair cells resting upon fibrillæ which are set into vibration vibrate with the fibrillæ and thus stimulate the nerve filaments which arborize around them.

(β) THE TELEPHONE THEORY OF WALLER makes the basilar membrane analogous to the telephone membrane which, as we know, may be thrown into vibrations of varying pitch, even reproducing a piece of music with its complex chords. The movements of the membrane here represent a resultant of all the impulses which affect it, and bodies resting upon such a membrane would likely be affected in a manner analogous to the way in which fine sand on a vibrating plate is affected—*i. e.*, thrown into an infinite variety of resultant patterns or combinations. This theory makes perception of different tones a perception of different patterns in the vibrating membrane.

3. THE SENSATION AND PERCEPTION OF SOUND.

a. The Range of Auditory Sensation and Perception.

1. **The Range of Pitch.**—(*a*) THE LOWER LIMIT is generally accepted as 16 vibrations per second.

(β) THE UPPER LIMIT is far beyond the upper note of the pianoforte, being usually somewhere in the octave between C^{vi} and C^{vii} above middle C—*i. e.*, representing between 16,704 and 33,408 vibrations per second (international pitch).

(γ) THE RANGE would thus be for the human ear 10 to 11 octaves. The range for one particular human ear would probably not exceed 9 or 10 octaves, because an ear that can perceive 33,000 vibrations per second would not perceive 16 vibrations per second as a continuous musical tone, but as a rapid succession of noises. Nine octaves may be accepted as the average limit for the individual human ear.

The range of perception of pitch *varies with age*. At the age of ten years the upper limit of pitch is about 40,000 per second (E^{vii}), while at the age of fifty years it has receded to about 30,000 per second (B^{vi}).

2. **The Range of Intensity.**—The lower limit of the range of intensity represents the acuteness of the hearing for faint sounds. Schafhäutl says: "A person of acute hearing can detect the sound made by a cork ball weighing one milligram (0.001 gm.) falling one millimetre (1 mm.) upon a glass plate 91 millimetres distant from the tip of the tragus and directly opposite to the meatus."

b. Judgments Based upon Auditory Sensations and Perceptions. Estimate of Distance and Direction of Source of Sounds.

This topic belongs to psychology. It may be briefly stated that the estimate of direction and distance is neither a sensation, a perception, nor a conception, but is the result of subconscious reasoning based upon a series of sensations, perceptions, and conceptions. The young child estimates direction and distance only after many sensations have been received. With increasing experience the estimation of direction and distance becomes gradually more perfect. At first the result of a conscious effort it becomes eventually subconscious or an automatic judgment.

VII. VISION.

INTRODUCTORY.

1. Physiologic Optics.
2. Comparative Physiology of Vision.
3. Embryology of the Human Eye.
4. Summary of the Anatomy and Histology of the Eye.

THE PHYSIOLOGY OF VISION.

A. Visual Optics: The Eye as an Optical Instrument.

1. Visual Refraction: The Refractive Apparatus of the Eye.
    - (a) *Application of the Laws of Refraction to the Mammalian Eye.*
    - (b) *Accommodation.*
        - (1) The Mechanism of Accommodation
        - (2) The Range of Accommodation.
    - (c) *Imperfections of the Refractive Apparatus of the Eye.*
2. Visual Mechanics: The Directive Apparatus of the Eye.
    - (a) *Monocular Fixation.*
    - (b) *Binocular Fixation and Convergence.*

B. Visual Sensation: The Eye as the Sense-organ of Vision.

1. Retinal Stimulation.
    - (a) *The Stimuli.*
    - (b) *The Irritability of the Retina.*
        - (1) Factors Involved in Retinal Irritability.
        - (2) Direct and Indirect Vision
2. Visual Sensations.
    - (a) *Fundamental Sensations.*
        - (1) Form.
        - (2) Intensity.
        - (3) Color.
    - (b) *Secondary Sensations.*
        - (1) After-images.
        - (2) Contrast.

- (*c*) *Color-blindness.*
  - (1) Complete Color-blindness.
  - (2) Yellow-blue Blindness.
  - (3) Red-green Blindness.
  - (4) Acquired.
  - (5) Normal Color-blindness.

3. VISUAL PERCEPTIONS AND JUDGMENTS.
   - (*a*) *Acuteness of Vision.*
   - *b*) *Visual Estimates.*
     - (1) Estimate of Distance.
     - (2) Estimate of Size.

1. PHYSIOLOGIC OPTICS.

a. Definitions.

(*α*) OPTICS *is the science of the phenomena of Light.* It comprises the study of the sources of light; the production of light; the propagation of light, and its various properties.

(*β*) LIGHT IS A MODE OF MOTION. The luminosity of a body is due to an infinitely rapid vibratory motion of its molecules, which, when communicated to the ether is propagated in all directions in the form of spherical waves, and this vibratory motion, transmitted to the retina, calls forth the sensation of vision (Ganot). The vibrations of the ether are transverse to the direction of the undulation—*i. e.*, they are *transversal vibrations.*

(*γ*) A LUMINOUS RAY is the direction of the line in which the light is propagated. Every luminous body emits divergent, rectilinear rays from all points of its surface, and in all directions.

(*δ*) A MEDIUM is any space or substance which light can traverse. Media may be transparent, or translucent.

Transparent media may be of various densities: glass is more dense than water, water more dense than air, and lower strata of air more dense than higher strata.

(*ε*) THE TERM PHYSIOLOGIC OPTICS may be applied to that portion of the general field of optics which deals with the transmission of light through the media of the organ of vision. Physiologic optics deals properly with refraction, though reflection is also frequently treated under this head.

b. Refraction.

PROP. I. When a ray of light passes from one medium into another medium in a line perpendicular to the plane separating the two media, the ray will continue its course in an unbroken straight line in the second medium.

Prop. II. When a ray of light passes from one medium into another medium in a line not perpendicular to the plane separating the two media, the ray will be broken at the surface of the second medium.

Prop. III. The plane determined by the two segments of the broken ray is perpendicular to the plane which separates the two media. *Corollary*: If the surface separating the two media be a curved one, the plane determined by the ray will be perpendicular to a plane tangent to the curved surface at the point of intersection of the ray.

Fig. 238

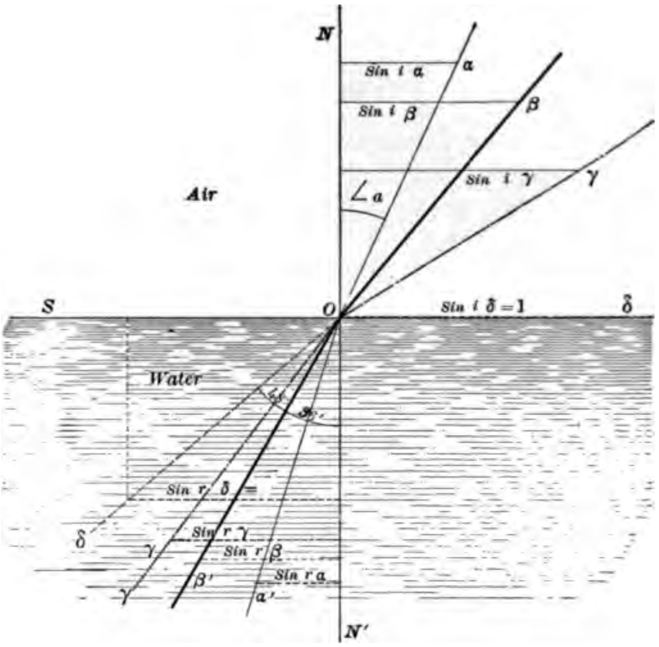


Diagram to illustrate refraction.

Prop. IV. If the second medium be denser than the first medium, the angle between the ray and the normal will be less in the second medium than in the first, and conversely.

Prop. V. The ratio between the sine of the angle of incidence and the sine of the angle of refraction is constant for any two media.[1]

---

[1] A *normal* is a line perpendicular to the surface of a medium at the point of incidence. The *angle of incidence* is the angle between the incident ray and the normal (as $\angle a$). The *sine of the angle of incidence* in Fig. 238 is the line *a N* measured upon the radius *a O*. The *angle of refraction* is the angle between the refracted ray and the normal $\angle a'ON'$. The index of refraction of any medium is the ratio between the sine of the angle of refraction in that medium compared with the sine of the angle of incidence when light passes from *air* into the medium in question. For example, *index* of refraction for water $= \frac{\sin i}{\sin r} = \frac{4}{3} = 1.33$.

$$\sin I : \sin R :: \sin i; \sin r.$$

As $\frac{\sin I}{\sin R}$ is a constant for any particular medium, it is customary o use μ to express this constant for air and each other medium, espectively.

Prop. vi. If a ray pass from any medium through a denser nedium which is bounded by two parallel planes, it emerges from he denser medium in a line parallel to its course before meeting hat medium. (See Fig. 239.)

Fig. 239

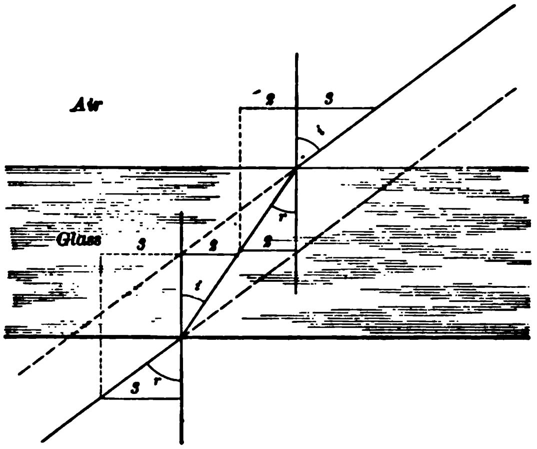


Diagram showing path of ray through a denser medium bounded by two parallel sides.

Prop. vii. If a ray pass from any medium through a denser nedium which is not bounded by two parallel planes, it emerges n a line not parallel to its original course, but invariably refracted oward the base.[1] (See Fig. 240.)

Prop. viii. The rays of light emitted from a luminous point in he optical axis will, on passing through a convex lens, be converged oward the optical axis—*i. e.*, more convergent or less divergent.[2]

---

[1] "A *prism* in optics is any transparent medium comprised between two plane faces inclined to ach other." (Ganot.) The *apex* of the prism is the line of intersection of the two planes. The ase of the prism is the boundary surface opposite the apex; unless otherwise defined, it is undertood to be perpendicular to a plane bisecting the angle of the apex. The *angle* of the prism is he angle between the bounding planes. The *angle* of *deviation* is the angle between the *incident* ay and the *emergent ray*.

[2] A *convex lens* is the optical equivalent of an infinite number of prisms standing base to base.
A *concave lens* is the optical equivalent of an infinite number of prisms standing apex to apex.
The *optical axis* is the line perpendicular to the plane of a lens and passing through its optical entre.
The *optical centre* is a point in the optical axis, any ray passing through which suffers no eviation.
The *principal focus* is that point at which parallel rays meet in passing through a convex lens. A concave lens has no real focus, but a virtual focus in the negative direction.
The *principal focal distance* is the distance between the optical centre of the convex lens and he principal focus.

PROP. IX. Rays of light emitted from a luminous point in the optical axis will, on passing through a concave lens, be diverged from the optical axis or will become more divergent or less convergent.

FIG. 240

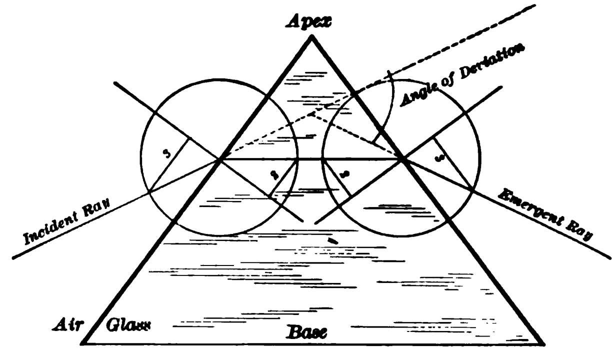
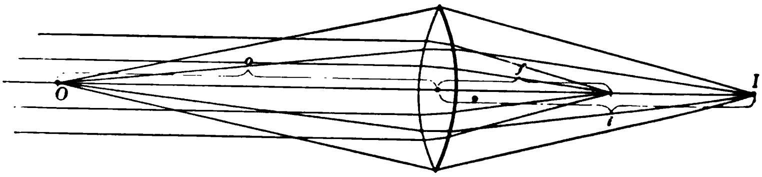


Diagram showing path of ray through a prism. Note that the incident ray is bent to the horizontal direction in the prism, and is refracted again on emerging still farther toward the base. If the two rays (incident and emergent) be extended in the dotted lines they will meet at an angle indicated in the figure. This angle is called the *angle of deviation*.

PROP. X. The sum of the reciprocals of the conjugate focal distances is equal to the reciprocal of the principal focal distance,[1] or $\frac{1}{o} + \frac{1}{i} = \frac{1}{f}$, or $f = \frac{oi}{o + i}$, when o = distance of object, i = distance of image, and f = principal focal distance.

FIG. 241



The relation of the conjugate foci to the principal focal distance.

The Simple Dioptric System.—The simple dioptric system is one in which the ray passes from one medium into a second medium of different refractive index, the surface of separation of the two media being a spherical surface. In the accompanying figure (Fig. 242) the spherical surface, s', s, p, s'', separates the medium m, whose refractive index is 1 from the medium m', whose refractive index is 1.5.

---

[1] *Conjugate Foci.*—If the source of light be near enough to the lens so that the rays are not parallel, but divergent, the lens will not bring them to a focus so soon as in the first instance; *e.g.*, rays from the point O would be focused at the point I. O and I are the conjugate foci, and o and i are the conjugate focal distances, respectively.

Note the following *cardinal points* of a simple *dioptric system:*

The centre of curvature of the spherical surface (n) in the nodal point.

That radius $n\ p$ which is the centre of symmetry of the dioptric system is called the *principal axis* of the system. In this axis lie the *first* and *second principal foci*, f and f', respectively. The point where the optical axis cuts the spherical surface (p) is called the *principal point*. The plane tangent to the spherical surface at this point is the *principal plane*. Planes perpendicular to the optical axis at f' and f are called the *first* and *second principal focal planes*, respectively.

1st. The ray $r\ s$ meeting the spherical surface perpendicularly will not be refracted at s, but will pass on through the nodal point.

2d. The ray $r'\ s'$ parallel to the principal axis in the first medium is refracted at the spherical surface and cuts the principal axis at f'—it passes through the second principal focus.

FIG. 242

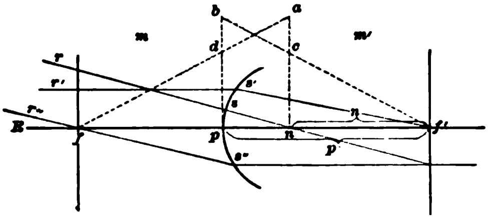


Diagram to show the cardinal points of a simple dioptric system.

3d. The ray $r''\ s''$ cutting the principal axis at f in the first medium (m) is refracted at s'' and traverses the second medium parallel to the principal axis.

2. COMPARATIVE PHYSIOLOGY OF VISION.

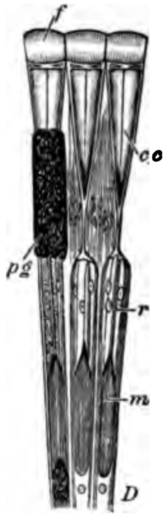
The most primitive manifestation of sensitiveness to light is that manifested by most unicellular organisms. Most unicellular plants gather upon the best illuminated side of an aquarium. Most multicellular algæ show sensitiveness to light either by movements of the plant as a whole or by movements of the chlorophyll grains within the plant cell. One can recall various examples of light stimulation —heliotropism—in higher plants. But plants have no specialized organs responsive to light; simply primordial protoplasm and the green pigment chlorophyll.

Many *protozoa* show a sensitiveness to light. Pelamyxa and Pleuronema, amœba-like animals, both contract all pseudopodia when light falls upon them. If one side of an aquarium is in deep shade these protozoa present in the aquarium will always be found there.

Many *cœlenterata* possess eye spots, which must be recognized as the most primitive organ of vision. The eye spots are simply patches of pigment which are more sensitive to light than is protoplasm generally.

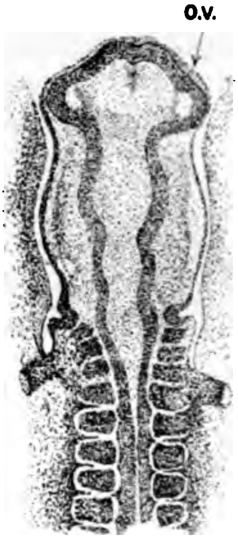
Echinoderms possess these primitive eyes in a very simple form. The eye spots at the end of a starfish's arms consist of a group of little invaginated pits, the cells of which are developed from a red pigment, and are in communication with the nerve ring through special sensory nerve fibres.

FIG. 243



Part of the compound eye of *Phryganea*, an anthropod. The retinal cells are seen to be united into a retinula, *r*, which is differentiated into a rhabdom, *m*, posteriorly; *c. c.* crystalline cone; *f*, facet of compound eye; *pg*, pigment. (From Bell, after Grenocher.)

FIG. 244



Chick. Forty-eight hours. (Kölliker.)

Turbellarians (*vermes*) have eyes in which the pigment-containing cells are differentiated from the sensitive cells. Some of these low worms have several hundred eyes, but the higher worms, as represented by the polychætæ, have a pair in each segment, each eye having a lens, a gelatinous vitreous humor, a layer of rods, and a layer of pigment. The common earthworm is blind.

The *molluscs* which are not blind have more primitive eyes than the higher worms. The *cephalopod* mollusc, however, has a highly developed eye, comprising a cornea, a lens, a ciliary body, a retina with internal and external layers, a pigment layer (choroid), an optic nerve. The eye is subspherical in shape, and is protected by spherical fibrous layers similar to the sclera of a vertebrate's eyes.

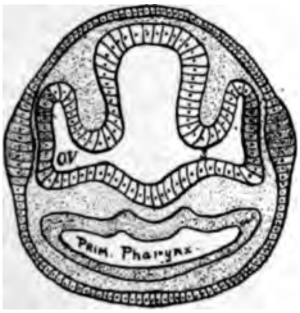
The *arthropoda* show a remarkably perfect development in another direction—in the compound eye. The highest crustacea and insecta possess a pair of these eyes, each having many hundred facets, each with its minute lens (corneal facet), its pigment sheath, and its retinule homologous to retina of a simple eye (Fig. 243).

The *vertebrata* all have eyes not very unlike those of man, which may be taken as a type of vertebrate eye.

3. EMBRYOLOGY OF THE HUMAN EYE. (Hertwig's Summary.)

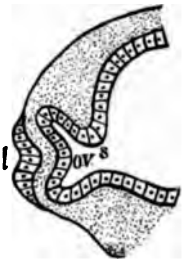
1. The lateral walls of the primary forebrain vesicle are evaginated to form optic vesicles (Figs. 244 and 245).

FIG. 245



Cross-section head of fish embryo. (Balfour.)

FIG. 246



From forty-eight-hour chick. (Marshall.)

2. The optic vesicles remain united by means of a stalk, the future optic nerve, with that part of the primary forebrain vesicle which becomes the Thalamencephalon.

3. The optic vesicle is converted into the optic cup through the invagination of its lateral and lower walls by the fundaments of the lens and the vitreous body.

4. At the place where the lateral wall of the primary optic vesicle encounters the outer germ layer, the latter becomes thickened, then depressed into a pit and finally constricted off as a lens (Figs. 246, 247 and 248).

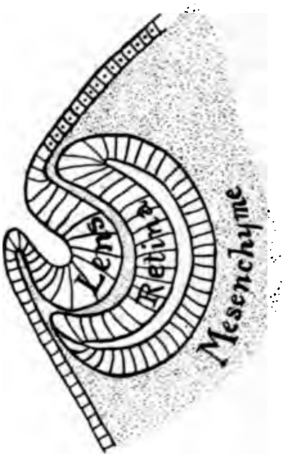
5. The cells of the posterior wall of the lens vesicle grow out into the lens fibres; those of the anterior wall become the lens epithelium (Figs. 251 and 252).

6. The fundament of the lens is enveloped at the time of its principal growth by a vascular capsule (tunica vasculosa lentis), which afterward entirely disappears except as given in 7.

7. Its anterior part becomes the transparent anterior part of the lens capsule (Fig. 251).

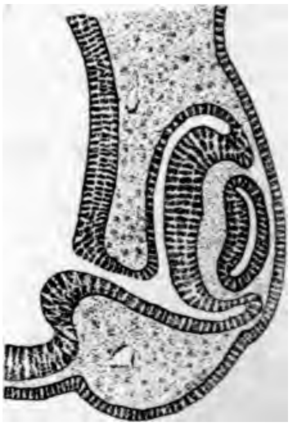
8. The development of the vitreous body is associated with the formation of the choroid fissure (Figs. 249 and 250).

FIG. 247



Horizontal section, fifty-four-hour chick. (Kölliker.)

FIG. 248



Cross-section, sixty-four-hour chick. (Marshall.)

9. The optic capsule has double walls (inner and outer epithelial), which are continuous with each other at the opening of the cup around the lens and along the choroid fissure (Figs. 247, 248, and 249).

FIG. 249

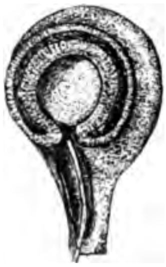
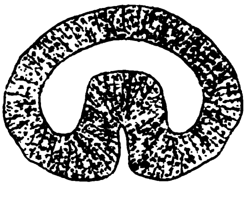


Diagram showing choroid fissure.

FIG. 250



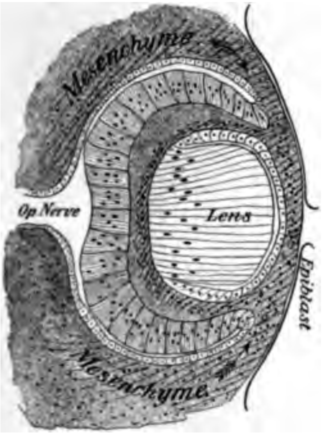
Cross-section, distal part of optic nerve of thirteen-day rabbit. (Minot.)

10. Mesenchymic cells migrate in between the lens and somewhat closely applied epidermis to form the cornea and Descemet's membrane, the latter being separated from tunica vasculosa lentis by a fissure—anterior chamber (Figs. 251 and 252).

11. The optic cup is differentiated into a posterior part within hich its inner layer becomes thickened and constitutes the retina nd an anterior part which begins at the ora serrata, becomes much ore reduced in thickness and extends over the front surface of the ns, growing into the anterior chamber of the eye until the originally ide opening of the cup is reduced relatively to the size of the pupil.

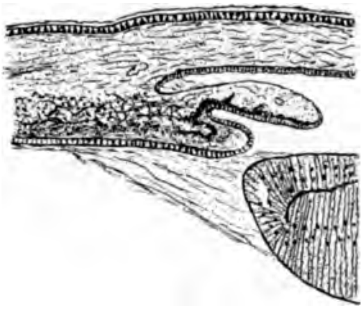
12. The anterior attenuated portion of the cup is, in turn, divided nto two zones of which the posterior zone becomes folded at the quator of the lens to form the ciliary processes, whereas in front it emains smooth, so that in the whole cup three parts may be disnguished: Retina propria, Pars ciliaris retinæ, Pars iridica retinæ Fig. 252).

FIG. 251



Horizontal section, sixty-four-day rabbit. (Note invasion of mesenchyme.) (Kölliker.)

FIG. 252



From section of eye of thirteen-day chick.

13. Corresponding to the three portions of the epithelial optic cup, e adjoining mesenchymal envelope (choroid) takes on somewhat ifferent conditions, as: (*a*) choroid proper; (*b*) connective-tissue troma of ciliary body and ciliary muscles; (*c*) connective-tissue troma of iris and muscles of iris.

14. The skin surrounding the cornea becomes infolded to form e upper and lower eyelids and the nictitating membrane (rudientary in man as the plica semilunaris).

15. The epithelial layers of the edges of the two eyelids grow gether in the last three months of development, but become sepaated again before birth.

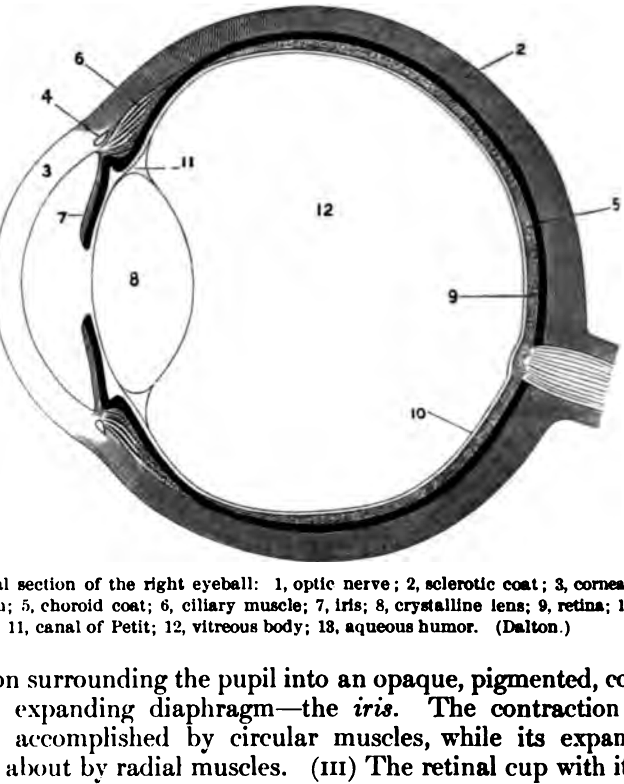
16. That part of the central nervous system between the retinal up and the thalamencephalon is the fundament of the optic nerve. he fibres of the nerve originate in the thalamencephalon and grow utward toward the retina through optic-nerve fundament.

4. SUMMARY OF THE ANATOMY AND HISTOLOGY OF THE EYE.

The following features of the anatomy of the eye are of special importance in the discussion of the function of the organ:

1. The eye is nearly spherical in form and possesses three coats: (I) A very dense, strong, outer coat—the *sclera*, modified anteriorly into a transparent *cornea* (Fig. 253, 2, 3). (II) A very vascular middle layer—the *choroid*, pigmented to a brownish-black color internally. Anteriorly this coat has an aperture—the *pupil*—and is modified in the region surrounding the pupil into an opaque, pigmented, contracting and expanding diaphragm—the *iris*. The contraction of the pupil is accomplished by circular muscles, while its expansion is brought about by radial muscles. (III) The retinal cup with its outer layer of pigment cells and its inner cerebroneuroepithelial layer. The *retina* is modified anteriorly, possessing a ciliary and an irideal portion which line the ciliary body and iris, respectively.

FIG. 253



Horizontal section of the right eyeball: 1, optic nerve; 2, sclerotic coat; 3, cornea; 4, canal of Schlemm; 5, choroid coat; 6, ciliary muscle; 7, iris; 8, crystalline lens; 9, retina; 10, hyaloid membrane; 11, canal of Petit; 12, vitreous body; 13, aqueous humor. (Dalton.)

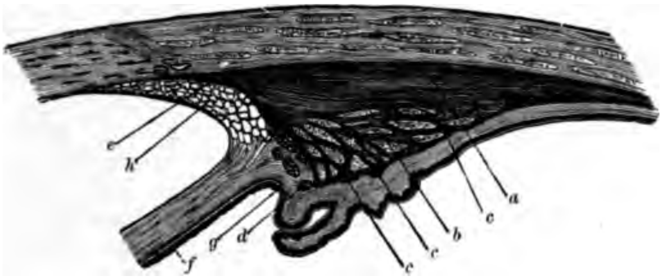
2. The eyeball is occupied by the following *refractive media of the eye:* (I) the *lens just behind the iris;* (II) the *aqueous humor* between the lens and the cornea; (III) the *vitreous humor* back of the lens.

3. The lens is held in position by the *suspensory* ligament, whose radiating fibres pass out and come into intimate contact with the pars ciliaris retinæ.

4. The *ciliary body* (Fig. 254) consists essentially of two sets of muscle fibres: (I) the *meridional fibres*, which extend from the annular tendon (Fig. 254, *e*) backward, gradually merging into the stroma of the choroid as indicated in the figures; (II) the *annular fibres*, which form a ring around the inner margin of the ciliary body.

5. The *retina* presents an outer layer of black pigment cells and an inner layer which represents the end organ of vision (Fig. 255). The inner layer is subdivided into a neuroepithelial and a cerebral layer. (I) The *neuroepithelial layer* comprises, besides a supporting epithelium (not shown in the figure) an epithelium sensitive to light. These specialized cells remind one strongly of the fila olfactoria.

FIG. 254



Section of the ciliary region of the eye in man: *a*, meridional muscular fasciculi of the musculus ciliaris; *b*, deeper-seated radiating fasciculi; *c*, *c*, *c*, annular plexus; *d*, annular muscle of Müller; *f*, muscular lamina of the posterior surface of the iris; *g*, muscular plexus at the ciliary border of the iris; *e*, annular tendon of the musculus ciliaris; *h*, ligamentum pectinatum. (After Foster.)

The rods especially present the elements of a typical neurone: the afferent member (*a*), the body (*b*), and the efferent member (*e*). The *cones* are not very different (Fig. 255). The efferent member of these epithelial neurones arborize in the *outer reticular layer* with the neurones of the cerebral layer. Like the mitral cells of the olfactory lobe (*q. v.*), these neurones of the second order arborize with several of the epithelial neurones. (II) The *cerebral layer* consists of two series of neurones whose cell bodies form the inner nuclear layer and the ganglion-cell layer. These two series of neurones differ slightly as to the disposition of their parts. Those which connect with the cones arborize with the ganglion cells in the inner reticular layer; those which connect with the rods arborize around the bodies of the ganglion cells in the ganglionic layer. The neuraxones of the ganglion cells pass along the inner surface of the retina—*i. e.*, next to the vitreous humor—to join with the fibres making the optic nerve.

6. The eyeball rests in a bony socket on a bed of fat. It is provided with lids, lashes, and brows, and a lacrymal apparatus by way of protection; and with four straight and two oblique muscles to direct it. The straight muscles are the superior, external, inferior, and internal recti. The oblique muscles are the superior and inferior oblique.

FIG. 255

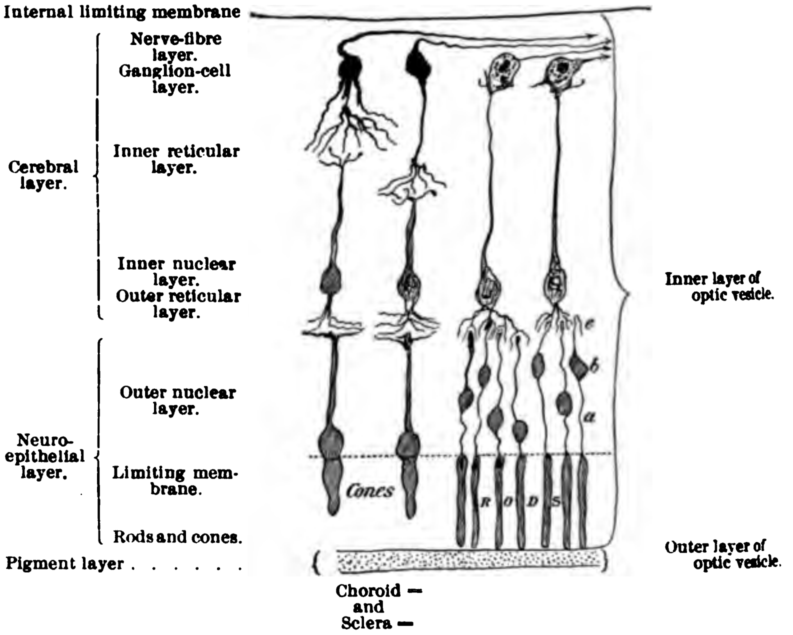


Diagram showing the neuronal structure of the retina. Note that the upper part of the figure is that which is next to the vitreous body, or the inner surface of the retina, while the lower part is the other surface of the retina. (Cajal's figure, somewhat modified.)

THE PHYSIOLOGY OF VISION.

If the student has mastered the general principles of refraction, and has familiarized himself with the structure of the eye, he is ready to consider the function of the organ.

Vision comprises two distinct phases of activity: (I) *Optical*, in which phase the eye as an optical instrument focuses upon the retina images of objects; (II) *Sensory*, in which the sensorium is made conscious of the form and color of the image through the neuro-epithelial cells—rods and cones—and the two orders of sensory neurones.

. VISUAL OPTICS: THE EYE AS AN OPTICAL INSTRUMENT.

Possessing a lens, with an adjustable focal distance, a diaphragm ith an adjustable aperture, a pigment lining for absorption of ispersed light, and a screen for the reception of the image, the eye ust at once be recognized as a typical optical instrument. Used s it is for viewing distant objects whose images are infinitesimal ompared with the objects, the eye resembles a telescope. But the djustable diaphragm in front of the lens and the screen for the eception of the image are points which make it more strongly esemble the photographic camera.

All of the optical instruments consist of two distinct mechanisms: i) *a refractive apparatus* for focusing the rays of light; (II) *a directive pparatus* for directing the axis of the instrument at the object whose mage is to be viewed.

1. VISUAL REFRACTION: THE REFRACTIVE APPARATUS OF THE EYE.

Before entering upon the consideration of this topic it might be nteresting to note that the mechanical and thermal stimuli of one's nvironment are quite unmodified preparatory to their stimulation f the sensory end organs, and the pressures and tensions and temerature act directly upon the sense organs transmitted practically nmodified through the superficial layers of the cuticle. The chemical gents, however, which serve to stimulate the sensory nerves of mell and taste must enter into solution before the end organs are timulated. Furthermore, the vibrations of ponderable matter must e condensed and intensified by the transmitting apparatus of the ar before they can sufficiently stimulate the end organs of hearing.

Finally, the vibrations of the imponderable, luminiferous ether can nly be recognized as light by the primitive eye spots of the cœlenteates and echinoderms. Nature has, through the lapse of the ages, volved a visual sense organ which is able to recognize not only the ifference between light and darkness, but also to perceive the form nd color of distant objects. In order to accomplish this, rays of ight are focused into a clearly defined image through the refractive pparatus of the eye.

a. Application of the Laws of Refraction to the Mammalian Eye.

The dissection of an eye reveals several refractive media (corea, aqueous humor, lens, and vitreous humor) and several curved surfaces bounding this media. In determining the focal distance of a lens one must know the radius of curvature and the refractive index. In determining the focal distance of a system of refractive media and surfaces one must know (I) the radius of curvature of each surface, (II) the refractive index of each medium, and (III) the location of their cardinal points upon the principal axis of the system.

The retina receives its light through a system of media and surfaces, as indicated in the following table:

MEDIA.	INDEX OF REFRACTION.	SURFACE.	RADIUS.
Air	1.000		
Cornea	1 3367	Anterior corneal.	7.829 + mm.
Aqueous humor	1.3365	Posterior corneal.	7.829 – mm.
Lens	1.4371	Anterior.	10.0 mm.
Vitreous humor	1.3365	Posterior.	6.0 mm.

This array of media and surfaces would seem to make a problem too intricate to solve with the means at our disposal. Notice first that the anterior and posterior corneal surfaces have the same radius of curvature—*i. e.*, though curved surfaces, they are parallel and form a case under the following theorem: "If a ray pass from any medium through a denser medium which is bounded by two parallel planes, it emerges from the denser medium in a line parallel to its course before entering that medium." It is customary at this point to take the anterior surface of the cornea as the first refractive surface and $\mu = 1.3365$.

Notice that the index of refraction of the aqueous humor and vitreous humor are the same. It is now evident that we have to deal with three media (air, aqueous or vitreous humor, and lens) with three surfaces, viz., anterior corneal surface, anterior and posterior lens surfaces, whose radii are 7.829, 6 and 10, respectively. But even this great step toward simplifying the problem leaves us with a long road before us unless we can find a short cut. "It has been shown mathematically that a complex optical system consisting of several surfaces and media, centred on a common optical axis, may be treated as if it consisted of two surfaces only."[1] The location of these surfaces and of the cardinal points is given as follows by Landolt:

1. **The Normal Eye.**—The point *r* (Fig. 256) where the principal axis cuts the cornea is 22.8237 mm. from the second principal focus *f′* (the retina); *C*, the centre of curvature of the cornea; *s*, the point where the optical axis cuts the anterior surface of the lens, is 3.6 mm.

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[1] Foster, Text-book of Physiology, 1891, vol. iv. p. 9.

from *r*, the point where the optical axis cuts the posterior surface of the lens 7.2 mm. from *r*; *l*, the centre of curvature of anterior surface of lens; *l'*, the centre of curvature of posterior surface of lens.

2. **The Accurate Mathematic Reduction.**—The reduction referred to in the text above is represented by the two refractive surfaces with nodal points *n* and *n'*, radii of 5.215 mm. each, and cutting the optical axis at *p* and *p'*, located 1.7532 mm. and 2.11 mm. respectively from *r*.

3. **The Final Approximate Reduction.**—Note that *p* is less than 0.36 mm. from *p'*. One may assume *one nodal point N*, and *one refracting surface* between the computed ones, cutting the principal axis at *P*, and introduce an error too slight to be considered. But this brings us back to the "*simple dioptric system,*" already described.

Fig. 256

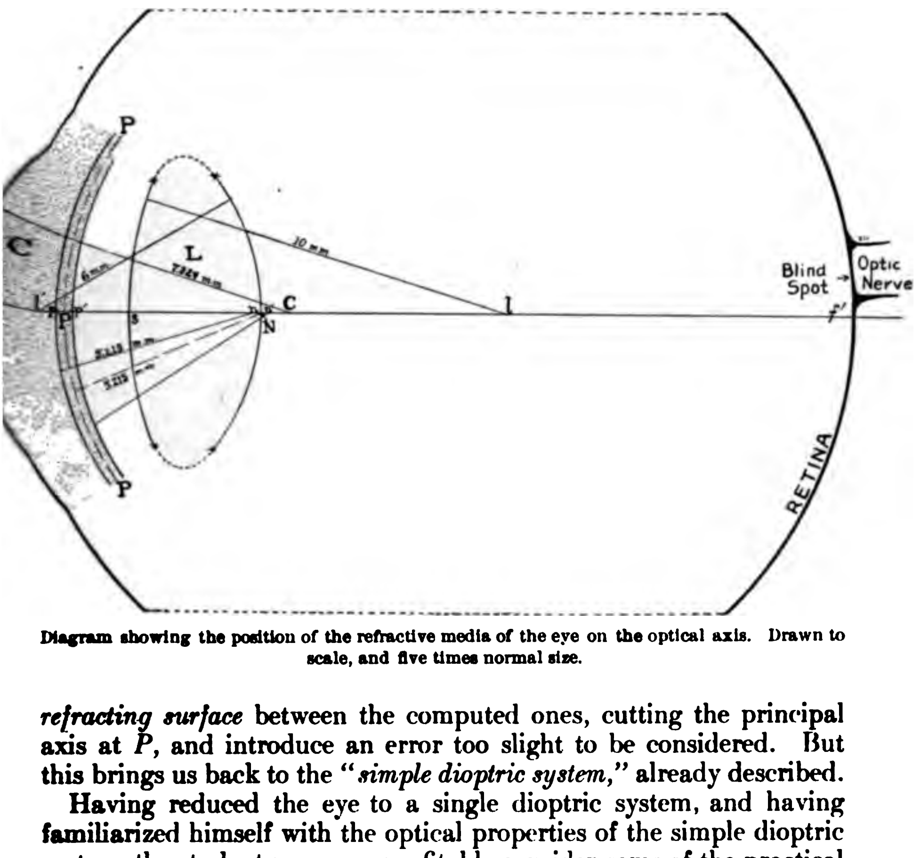


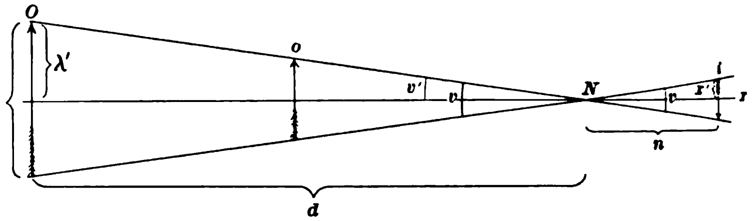
Diagram showing the position of the refractive media of the eye on the optical axis. Drawn to scale, and five times normal size.

Having reduced the eye to a single dioptric system, and having familiarized himself with the optical properties of the simple dioptric system, the student may now profitably consider some of the practical applications of the optical properties.

4. **The Visual Angle.**—The visual angle is the angle which the object subtends at the nodal point—the angle *v* in Fig. 257. It is evident that the object *o* subtends the same angle as does the object

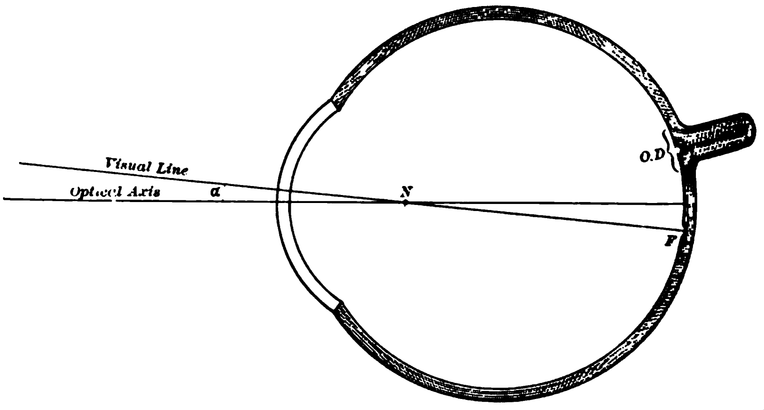
O, and its length measured upon its distance gives the same visual angle, *v*; to be concrete, a cent held near enough to the eye could obscure a great edifice which is some distance away. Helmholtz determined the minimum visual angle to be 50 seconds. The maximum visual angle for direct and distinct vision is not great, say 3 to 5 degrees, but varies considerably with different individuals. The maximum visual angle for indirect vision is very great—for a white or luminous body being 50 to 60 degrees to the median side of the *line of vision*, 60 degrees above the line of vision, 70 degrees below the line of vision, and more than 90 degrees laterally from the line of vision, or over 150 degrees in the horizontal plane and about 130 degrees in the vertical plane. (See perimeter chart, Fig. 264.)

Fig. 257



Illustrating the *visual angle* (*v*) and the relation of the distance (*d*) to the length of the object (*o*) and image (*i*). *N*, the nodal point; *n*, the focal distance, the image being on the retina.

Fig. 258



Illustrating the optical axis and visual line. Angle *a* = 5 degrees; *F*, fovea centralis, or central pit of the macula lutea; *O.D.*, optic disk, or blind spot, marking the entrance of the optic nerve.

5. **The Line of Vision.**—Reference has been made to the line of vision. This is the line determined by the nodal point of the eye and the "point of fixation," or the point at which the eye is directed. Within the eye the extended line of vision as just defined

meets the retina in the centre of the macula lutea, in the *fovea centralis*. This line of vision does not lie in the *mathematic axis* of the cornea, lens, and vitreous humor, but crosses the mathematic-optical axis in the nodal point. It meets the retina between the fovea and optic disk, and passes through the centre of the cornea while the line of vision passes the cornea to the median side of the *optical axis*. The angle between the optical axis and the line of vision is one of about 5 degrees. (See Fig. 258.)

6. **The Size of the Retinal Image.**—Given the distance of the object (d), the size of the object (λ), and the distance from the nodal point to the retina (n), it is very simple to compute the size of the retinal image (x) from the equation $x : n = \lambda : d$, or $x = \frac{n\lambda}{d}$; n is a constant and equals 1.5677 cm.; then $x = 1.5677 \frac{\lambda}{\mathrm{d}}$. Express λ and d in centimetres and x will be in centimetres.

To determine the minimum width of the retinal image which is able to excite the sense of vision—*i. e.*, which the subject is able to see—put a black dot 0.2 mm. in diameter upon a white card and move it away from the eye until it can just be seen. Substituting 0.2 mm. for λ in the formula $x = \frac{15.67 \times 0.2}{d \text{ (in mm.)}}$, gives the diameter in millimetres of the smallest visible image.

7. **The Optic Disk, or Blind Spot.**—(*a*) THE LOCATION OF THE BLIND SPOT may be determined as follows (Marriotte's experiment): On a white card make a black cross and a circle about three inches apart. Closing the left eye, hold the card vertically about fourteen inches from the right eye so as to bring the cross to the left side of the circle. Look steadily at the cross with the right eye, when both the cross and the circle will be seen. Gradually bring the card toward the eye, keeping the axis of vision fixed upon the cross. At a certain distance the circle will disappear—*i. e.*, when its image falls upon the entrance of the optic nerve. On bringing the card nearer the circle reappears, the cross, of course, being visible all the time.

(β) THE OUTLINE OF THE BLIND SPOT may be determined as follows: Make a cross on the centre of a sheet of white paper and place it on the table about 30 centimetres from the cornea; close the left eye and look steadily at the cross with the right eye. Wrap a penholder in white paper, leaving only the tip of the pen point projecting; dip the latter in ink, or dip the point of a white feather in ink, and, keeping the head steady and the axis of vision fixed, place the pen point near the cross and gradually move it to the right until the black becomes invisible. Mark this spot. Carry the blackened point still farther outward until it becomes visible again. Mark this outer limit. These two points give the outer and inner limits of the blind spot. Begin again, moving the pencil first in an upward, then in a downward direction, in each case marking where the pencil becomes invisible. If this be done in several diameters an outline of the blind spot is obtained, even little prominences showing the retinal vessels being indicated.

(γ) THE SIZE OF THE OPTIC DISK may be readily determined by using the formula given above. Let x equal the long axis of the disk; d the distance from the nodal point to the sheet of white paper upon which the map of the white disk was drawn.[1]

b. Accommodation.

When the normal eye at perfect rest is directed at a distant object, the image is formed upon the retina—*i. e.*, the principal focal distance of the resting normal eye is 15.677 mm. As long as the object is sufficiently distant to make the rays of light from any point of the object practically parallel, the image is focused upon the retina of the normal eye without any change in the dioptric system of the eye—*i. e.*, with the elements of the dioptric system in the state of rest. The minimum distance to which an object may be brought without requiring a readjustment of the elements of the dioptric system is found to be about 6 m. (20 ft.). In practical ophthalmology this distance is taken as infinity (∞) in all those problems which involve parallelism of the incident rays.

If an object be moved along the optical axis or visual line of a dioptric system the focus will recede and the distance from the nodal point to the image will exceed the focal distance—*i. e.*, the image would be formed behind the retina. The image can be seen only when it is focused upon the retina. The eye possesses the means of adjusting itself to this requirement. The process of adjustment is called *accommodation.*

The image is focused upon the retina by varying the radius of curvature of the crystalline lens. The process of accommodation is the process of varying the curvature of the crystalline lens.

1. **The Mechanism of Accommodation.**—Various ways have been suggested by which the radius of curvature of the lens might be increased; the theory now generally accepted is that of Helmholtz:[2]

(*a*) **The Change in the Lens** is accomplished through the interaction of two forces: (I) the elasticity of the lens body, and (II) the contraction of the ciliary muscles. The lens when left to itself tends to become more spherical than it is when the eye is at rest; it tends by its elasticity to take the position l'; but the elasticity f the choroid coat through its relaxed ciliary muscles (m) and through ts inelastic tendons the "suspensory ligaments" (*S.L.*) exert a still tronger tension in the opposite direction and the lens is flattened nd drawn down to the position l. All that is necessary to cause he lens to take the position l' or any position between l and l' is for he ciliary muscle to contract, thus relaxing the suspensory ligaments nd allowing the lens to become by its own elasticity more nearly pherical. There are two ways of convincing one's self of the increase convexity of the lens during accommodation.

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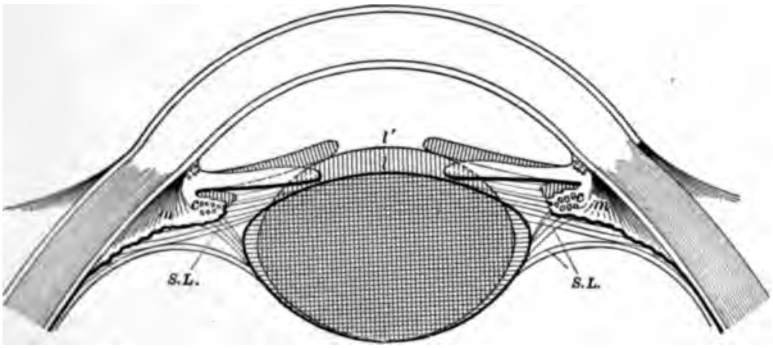
[1] This distance equals the distance of the cornea from the paper plus 7 mm.

[2] First published in his Handbuch der physiologischen Optik, Heidelberg, 1866. Given in full in the last edition, edited by Arthur König, Berlin, 1896, pp. 130-166.

(a) THE DIRECT OBSERVATION OF THE CHANGE in the lens may e accomplished by looking from the side at the margin of the iris hen the eye of the subject is at rest—*i. e.*, focused upon a disant object. Let the subject suddenly change focus to a very near ject. The iris at the margin of the pupil will be seen to advance ward the cornea—pushed out by the lens. (See Fig. 259.)

FIG. 259

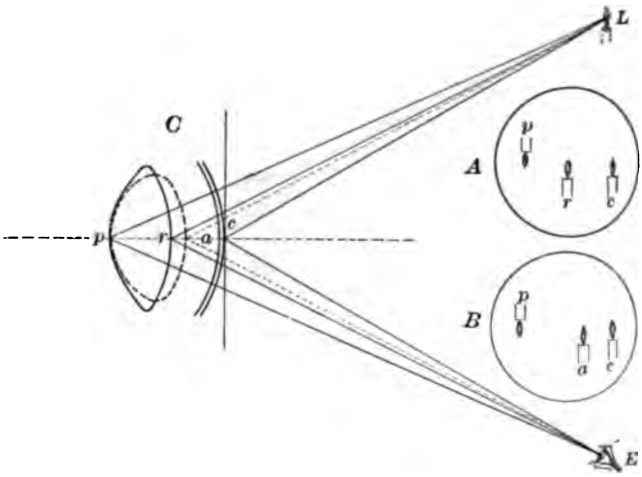


howing the mechanism of accommodation. The horizontally shaded lens and the unshaded s show the position of the parts when at rest; the vertically shaded lens and iris show the posi n during accommodation for a near point. m, meridional muscle; c, circular muscle; *S.L.*, spensory ligament. (After Landolt.)

(β) THE INDIRECT OBSERVATION OF THE CHANGE may be accomished by looking diagonally at the subject's eye (Fig. 260, E), while light shines upon the eye from position L. The light will be reected from the anterior surface of the cornea, from the anterior surce of the lens, and from the posterior surface of the lens. When e lens is at rest the images will have to each other the relation incated in A, Fig. 260. If the subject accommodates, the middle age will move over toward the corneal image, as shown in B to a, ig. 260. The geometric figure shows how this change is brought out. Utilizing the principle, Helmholtz contrived an instrument hich he called the *Phakoscope*.

(b) **The Pupil Changes its Position** both passively and actively. s passive change, as it is pushed out by the bulging lens, has been already referred to. Its active change may be observed readily if one looks into the eye of a subject from the front, while the subject directs his vision to some distant object. Let the subject then look at a near object and the observer will see the pupil contract. This contraction is accomplished through the action of circular irideal muscles. The reason for the contraction of the pupil is next to seek. One looks at near objects in order to study their detail of structure; detail of structure can be brought out in an image of a dioptric system only when the spherical aberration, caused by the margins of the lens, is corrected. Work with a microscope soon impresses the fact that for high magnification (near vision) clear definition is possible only when the diaphragm admits rays to the centre of the lens exclusively. In the same way in near vision, the eye, by contracting its pupil (its iris diaphragm), brings about a clear definition of the image.

FIG. 260



Showing the change in the position of the image reflected from the anterior surface of the crystalline lens: *A*, position of images when the eye is at rest; *B*, position of images when the lens is more spherical through accommodation; *C*, a geometric figure showing the reason for the change in position; *E*, observer's eye; *L*, candle.

(*α*) The Most Important Function of the Iris is that which it performs in conjunction with the lens in the act of accommodation.

(*β*) The Relation of the Pupil to Accommodation is not the sole function of the iris. This changeable diaphragm serves also an important purpose in cutting out an excess of light. If one shade the eyes of a subject and then suddenly allow the light to strike them, the pupil will be observed to contract through the action of the circular muscles of the iris. This is a reflex act in response to e overstimulation of the retina, the optic nerve acting as a sensory ment, while the oculomotorius is the motor element of the reflex arc.

(γ) In this connection it may be added that THE IRIS IS AN IMPORNT CLINICAL INDEX OF CERTAIN CONDITIONS. The sympathetic rvous system, from the ciliospinal centre supplies the radiating res; so that anything which profoundly affects the sympathetic stem will cause a dilatation of the pupil. A strong emotion, pecially fear, causes a dilatation of the pupil. In deep chloroform rcosis, or in the last stage of asphyxia, the pupils dilate. The rdriatic drugs (belladonna, atropia, etc.) cause dilatation. Paralysis the oculomotorius causes dilatation. The pupil contracts norally during sleep, during accommodation, and strong light. When e cervical is paralyzed, when a myotic drug—as physostigmine eserine—is applied locally or opium taken internally, the pupil so contracts.

2. **The Range of Accommodation.**—This is the amount of fractive change induced by the eye in adjusting for its point of arest vision—*punctum proximum*—after it has been at rest—*i. e.*, ter it has been adjusted to its point of farthest vision—its *punctum motum.*

(*a*) **To Determine the Punctum Proximum** one has only to record in etres the distance from the cornea to the printed page, when the bject can see the lines perfectly clearly; that is, without noticing y blurring of the letters. Suppose this distance be 10 cm., then one ites punctum proximum = 0.1 metre.

(*b*) **To Determine the Punctum Remotum** let the subject look at object 6 metres away. If he can make out the details of the ject and can read letters 1 cm. in height and with strokes 2 mm. width, one will credit him with a punctum remotum of *infinity*). If the subject cannot see distant objects, bring the object nearer til he can see its details of structure. Let us suppose that it must brought to a distance of 50 cm. before the subject can make out details, then one writes punctum remotum = 0.5 metre.

(*c*) **To Determine the Range of Accommodation.** Let R = the stance of punctum remotum, then the static refraction, or the fraction when the eye is at rest, may be represented by r, which is e reciprocal of the distance. Let P be the distance of the punctum oximum and p the maximum refraction of the eye. Let both r and be expressed in dioptres.[1] Let a be the range of accommodation pressed in dioptres. Then we have the simple equation $a = p - r$.

(*a*) IN THE NORMAL EYE (emmetropia) the punctum remotum is finity, r would therefore be 0, p for twenty years equals 10 D.

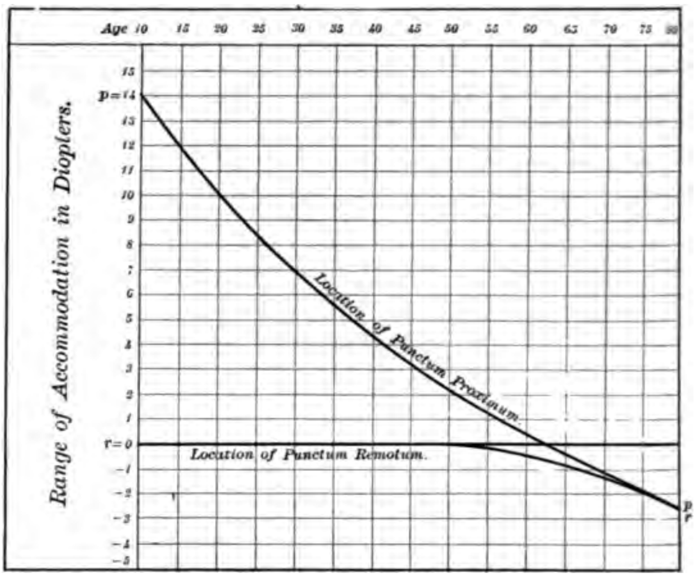
Lenses are now almost universally numbered according to the metric system. A lens with a al distance of 1 m. is called a 1 dioptre lens or 1 *D*. A lens with 50 cm. or ½ m. is called a 2 *D* s, and so on; 1/3 m. corresponding to 3 *D*, 1/4 m. to 4 *D*, 1/5 m. to 5 *D*, 1/8 m. to 8 *D*, 1/10 m. to 10 *D*, . to ½ *D* or 0.5 *D*, 4 m. to 0.25 *D*, 8 m. to 0.125 *D*, etc.

Applying the formula: $a = p - r = 10\text{ D} - 0\text{ D} = 10\text{ D}$. Normal range of accommodation for the age of twenty is 10 D.

(β) In the Myopic Eye the punctum remotum may not be more than 0.5 metre ($r = 2\text{ D}$); while the punctum proximum is probably not within 10 cm. ($p = 10\text{ D}$). The range of accommodation would therefore be $a = p - r = 10\text{ D} - 2\text{ D} = 8\text{ D}$.

(γ) In the Hyperopic Eye the punctum remotum is "beyond infinity," or negative. We must therefore express r as a negative quantity. The formula becomes $a = p - (-r) = p + r$. Suppose that the punctum remotum is 2 D. and the punctum proximum 10 D.; then $a = p + r = 10\text{ D.} + 2\text{ D.} = 12\text{ D.}$

Fig. 261



Curves showing the influence of age upon the location of the punctum proximum and the punctum remotum, and upon the range of accommodation. (After Landolt.)

(*d*) **The Influence of Age** upon the range of accommodation is well shown in the accompanying chart (Fig. 261). The average 10-year-old boy or girl has a range of ($a = p - r$) 14 D. At twenty-five years the range has decreased through a recession of the punctum proximum to ($a = p - r = 8 - 0$) 8 D. At forty-five years it is 3 D; at fifty years, 2 D; at sixty years, 1 D. Note that the punctum remotum begins to recede at fifty to fifty-five years, and at sixty years $p = +0.5$ and $r = -0.5$; so that $a = 0.5 - (-0.5) = 1$ D.

c. Imperfections of the Refractive Apparatus of the Eye.

It will be remembered that the sole function of the eye as a refractive apparatus is to focus rays from any object, near or far, upon the etina; that when the accommodative (focusing) apparatus is at rest he image of an object 6 m. or more distant is formed upon the retina n the normal eye ($f = i$). The distance of the image depends, then, pon the value of f. But the principal focal distance depends in turn pon the radius of curvature, the index of refraction, and the location n the optical axis of the elements of the dioptric system. In the ature of the case the index of refraction cannot change perceptibly. n the principal imperfections of the refractive apparatus of the eye he position of the elements of the dioptric system upon the optical pparatus is faulty. If the screen (retina) is too far back, the rays vill come to a focus before reaching the retina. The subject will ttempt to correct the difficulty by bringing the object near to the ye, thus increasing the conjugate focal distance until the image alls upon the retina. This bringing of the object near to the eye s a sign of a condition of the eye which has in consequence been alled "*near-sightedness.*" The oculists call this condition *myopia*, nd correct it by placing before the eyes concave or divergent lenses, vhich enable the subject to see distant objects.

The retina may be too close to the nodal point; that is, the eyeball nay be flattened in the anteroposterior diameter. In that case rays f light from a distant object would not be brought to a focus by he time they reach the retina. The subject will attempt to correct he difficulty by bringing into action the accommodative apparatus f the eye, thus bringing the focus nearer to the nodal point until it alls upon the retina and the object is clearly seen. This condition s called far-sightedness, or *hypermetropia*. The oculists correct it y placing before the eyes convex or convergent lenses, which enable he subject to see distant objects without the help of accommodation.

The radius of curvature of the cornea may be difficult in different neridians. If the radius is shorter in the horizontal than in the ertical plane, the rays which lie in that plane will be focused nearer o the nodal point than will those which lie in the vertical plane. It must be evident that the eye would, under such conditions, be uite unable to focus both horizontal and vertical lines at the same ime. Bringing the object nearer does not relieve the subject; using he accommodation does not help the condition.[1]

The most effective way of relieving the condition without artificial neans is for the subject to bring the eyelids very close together, eaving only a narrow horizontal slit. In this way all of the rays re cut out except those in one plane, and if these do not fall upon he retina when the eye is at rest the subject may bring the object nearer to the eye or may use the accommodation. This condition f the eye is called, by the oculists, *astigmatism*, and it is corrected by placing before the eyes convex or concave cylindric lenses, which increase the curvature of the refracting surface in one plane only. It is only necessary to adjust the axis of the cylinder at such an angle as to increase the curvature in the plane where it is smallest (or decrease it through the use of planoconcave cylinders in the plane where it is greatest) to put the dioptric system into approximately perfect condition.

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[1] It is held by some ophthalmologists, however, that a modified accommodative act may conract the ciliary muscles in one plane more than in another, and thus correct. or at least partially orrect, the condition.

2. VISUAL MECHANICS.

As the telescope or the camera must be provided with a directive apparatus, by means of which the direction of its optical axis may be changed, so the eye is provided with an apparatus for changing the direction of the line of vision. In directing the vision from one point or object to another the axis of the eye is turned upward, downward, outward, or inward, or is circumducted. In short, the axis of the eye has an absolutely universal motion within its limits.

a. Monocular Fixation.

The term monocular fixation is used to designate the mechanical adjustment of the eye to bring the image of the object upon the macula lutea, the most sensitive portion of the retina. If one study the movements of one eye (the other being shaded) he will find that it readily follows the movements of an object held in front of it, however quickly or through whatever angles or directions it may be moved by the observer. The directive apparatus of the eye consists of the six muscles named in the anatomic introduction, moving the eye about three different axes of rotation: (I) a horizontal axis about which the eye rotates upward and downward; (II) a vertical axis about which the eye rotates from right to left; and (III) a longitudinal axis which coincides practically with the physiologic axis or line of vision, and about which the eye rotates (slightly) when the oblique muscles are in action. These three axes are rather arbitrarily located. Inasmuch as the eye is a spherical body resting in a hollow spherical socket, and inasmuch as it rotates freely in any direction about the intersection of the three assumed axes, it is somewhat simpler to take a central *point of rotation* about which the eye may rotate in any direction whatsoever under the action of one or more of its six muscles. Waller's excellent diagram (Fig. 262) given in the accompanying figure will enable the student to interpret the mechanism of the directive power of the eye. Take, for example, the movement of the optical axis of the right eye outward or away from the median line in the horizontal plane. This movement is accomplished by the external rectus innervated by the sixth nerve. Again, take the movement of the axis of the eye upward in he vertical plane. It is evident that the superior rectus alone cannot accomplish this; but that that muscle must act in conjunction with he inferior oblique. In a similar manner movement vertically downward requires the combined action of the inferior rectus and the uperior oblique.

In general, the contraction of a single muscle causes a rotation of the eye in the direction indicated in the diagram for that muscle; while rotation in any other direction than the six which are indicated by the arrows requires the interaction of the two muscles, and frequently the co-ordinative influence of two nerves. To circumduct he eye, sweeping its axis around a circle requires the action of all of the muscles, acting two or three at a time; an action the exactness of adjustment and the complexity of co-ordination of which must compel the admiration of any student of mechanics.

FIG. 262

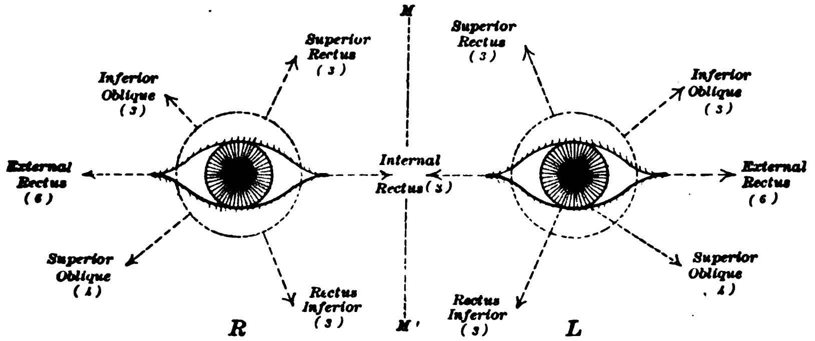


Diagram to illustrate the directions toward which the optical axis is directed or inclined by the contraction of the individual muscles. M M' is the median line; R, the right eye, and L the left one. The numbers in parentheses (3, 4, and 6) indicate the innervation of the muscle. After Waller.)

b. Binocular Fixation.

This expression is used to designate the co-ordinated binocular movement which results in directing the physiologic axes of *both* eyes upon the same object. If the object fixed by both eyes be a small one, its image falls upon the fovea centralis; if it be a large one, it will be disposed about that point symmetrically, as shown in Fig. 263, the lower part of the object being focused upon the upper segment of the two retinæ, and the right part of the object being focused upon the left part of the two retinæ; that is, upon the median segment of the right retina and the external segment of the left retina.

It is evident that we have to deal with a complex mechanical action: (I) with double monocular fixation, and (II) with convergence of the visual axes of the eyes. If one refers to Waller's diagram he can readily tabulate the muscles involved in directing the two eyes in any particular direction. If in Fig. 263 the object *O* move toward the right eye along the visual axis *O N F*, the fixation of the right eye will not need to be readjusted. If, however, the visual axis of the left eye *O N′ F′* follow the movement of the object, it will have to deflect to the right, thus making a greater angle (*L F O m*) with the median line (*m m′*) than existed before. This increase of the *angle of convergence* is brought about by the internal rectus. If through weakness or through paralysis this muscle is unable to rotate the eye far enough to bring the points *O*, *N′*, and *F* into a straight line, then the retinal image would not fall upon the field (*a′ b′ c′ d′*) and there would be a double visual sensation, "double vision," or *diplopia*. Failure for any other reason to produce perfect binocular fixation leads to the same derangement of vision. This is the principal—though not especially frequent—imperfection of the directive or mechanical apparatus of the organ of vision, and is often corrected by oculists through the use of prismatic lenses which bend the optical axis, bringing the image upon the proper field of the retina.

FIG. 263

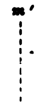


Diagram showing the symmetric correspondence of the retinal field. *N*, nodal point; *F*, fovea centralis. The observer is supposed to be looking down upon the optical apparatus from above. Note that the line *C D*, which is on the lower side of the object, is the upper side of the image; and that the line *B D*, which is the right side of the object, is the left side of the image, which brings it at the inner segment of the right retina and the outer segment of the left retina.

B. VISUAL SENSATION.

The Eye as the Sense Organ of Vision.

The retina is the end organ of vision; its function is to receive the impression of the image focused upon its surface by the optical apparatus and to transmit the impression to the brain. About all at can be said is that the lights, shades, and colors of the retinal nage start in the neuroepithelial cells metabolic changes which are nfluenced more or less by the action of the light upon the pigments n the associated tissues. The neuroepithelial cells are composed f an afferent element represented by the cones or rods of the external yer of the retina; that is, the scene of the metabolic changes referred above. The chemical changes start, along the afferent element endrite) toward the cell body, an impulse which is transmitted by e efferent element (neurite) to the first neurone of the cerebral yer of the retina, thence by the second neurone to the sensorium f the brain.

The phases of visual sensation which seem most profitable to discuss re retinal stimulation, retinal irritability, and visual sensations.

1. RETINAL STIMULATION.

a. The Stimuli.

(*α*) The Kinds of Stimuli which lead to visual sensation are imited normally to (i) diffuse light in its various colors and to ii) images of objects. In either case the stimulus is light, but t seems expedient, in view of what is to follow, to differentiate etween the light in general and images of objects. The retina, n common with all highly specialized tissues, responds to all timuli with the same general sensation. If one press upon the side f the eyeball, a ring of light will be seen upon the opposite segment f the retina. The retina is stimulated under the finger, but it is eferred to the opposite side. When a mechanical shock to the head makes one "see stars," these luminaries are real sensations due to the mechanical stimulus. Electricity may also produce the sensation of light.

Light being a mode of undulatory motion, it may vary in two ways: (i) in the number of vibrations per unit time, (ii) in the amplitude of the vibrations. The first variation is comparable to the variation in the pitch of sound and leads to the color scale; the second variation is comparable to loudness and is recognized in the intensity of the sensation.

(*β*) The Duration of the Stimulus may be very short. An electric spark whose duration is less than a millionth of a second is long enough to produce a sensation (Waller). The sensation which a stimulus calls forth is of much longer duration than the stimulus itself. This is made evident when one looks at a rapidly rotating wheel; a spoke occupies a particular position for only an infinitesimal fraction of time, yet it calls forth a sensation. In the position which the spoke takes during the next infinitesimal unit of time another sensation is induced; but the sensation of the previous stimulus persists and the two sensations blend. The result of this blending of the images of the rotating spokes is to produce the effect of a solid wheel. In a similar way if a luminous body be attached to the rim of the rotating wheel the sensation which it produces will not be a point of light, but a more or less elongated line of light. The faster the rotation of the wheel, the longer the arc of light, until finally the speed of the rotation may be great enough to extend the line of light around the whole circumference of the circle in a solid ring of light. Charpentier says that an interval of $\frac{1}{40}$ of a second must elapse between two flashes of light in order that both can be seen separately.

b. The Irritability of the Retina.

1. **Factors Involved in Retinal Irritability.**—(*a*) THE STRUCTURE OF THE RETINA bears an important relation to its irritability. The two kinds of neuroepithelial cells—the rods and the cones—are not equally distributed over the retina. There are no rods in the macula lutea; this portion of the retina possesses the cones only. The macula lutea is especially sensitive to the fine lines of images focused upon it—*i. e.*, it is the only portion of the retina from which one may receive a clearly defined image. That portion of the retina outside of the macula lutea is only faintly sensitive to form, but is very sensitive to light and responds to very slight modifications in the intensity of the stimulus.

(*β*) THE RETINAL PIGMENTS bear some relation to the irritability of the retina. Melanin, or fuchsin, is the brownish-black pigment which makes up the pigment layer of the retina. This pigment seems to form a stock from which other pigments may be replenished. *Rhodopsin*, or "*visual purple*," is found in the rods, and is, therefore, absent from the macula lutea. *Chromophanes* are red, green, and yellow oil globules found in the cones. The chromophanes are not found in the eyes of mammals.

(*γ*) VARYING IRRITABILITY OF DIFFERENT AREAS of the retina is probably due to varying distribution of the rods, cones, and pigments. The following facts are important in this connection: (I) The macula lutea is the area of clearest definition of form; it is, in fact, the only area sensitive to the fine structural details of an image. (II) The macula lutea possesses cones, but no rods, and in its most sensitive area—the fovea centralis—the cones are brought into special prominence by the thinning out of all the other elements. (III) The portion of the retina most sensitive to variations of the intensity of diffused light is that portion outside of the macula. (IV) The portion of the retina outside of the macula is richly studded with *rods*, and each rod possesses its supply of rhodopsin. (V) A solution of rhodopsin bleaches n the light. The retinal image may be actually "fixed" by treating, with 4 per cent. solution of potassium alum, the retina which has ust been removed immedialely after thorough exposure following rest in the darkness. The "fixed" image is called an *optogram.*

These facts seem to justify the conclusion that *the cones are the structures which receive form pictures and the pigmented rods are the structures which receive light and color impressions.*

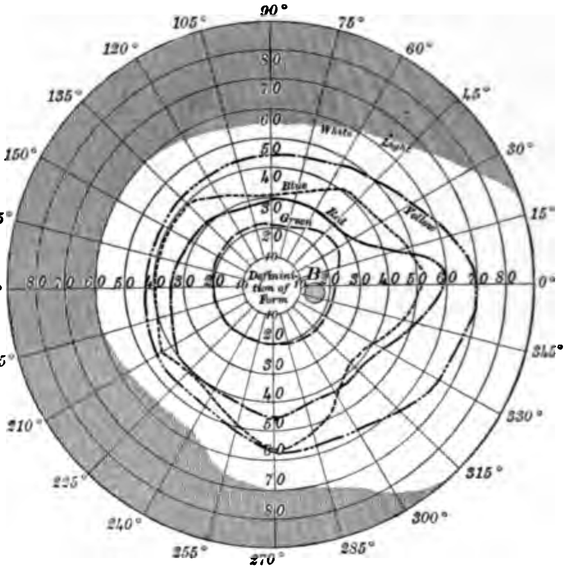
2. **Direct and Indirect Vision.**—These terms designate respectively he central field of clear definition and the surrounding field of ndistinct definition. One may get a very good idea of the difference between direct and indirect vision by holding before one eye (the other being shaded) at a distance of 30 cm. a printed page.

(*a*) DIRECT VISION.—Direct the line of vision at a small word; the surrounding words will be recognized for a distance of perhaps 2 cm. in any direction, but by studying the sensation very carefully, keeping one particular letter constantly fixed in the line of vision, that one letter is the only letter upon the page that is absolutely clearly defined. The image of that letter lies upon the centre of the fovea centralis; the two adjacent letters lie upon the slanting sides of the fovea; their definition is only slightly less distinct than that of the central letter. The form of the next adjacent words can be made out with sufficient clearness to enable the observer to say definitely what the words are, but he would be quite unable to detect any slight typographic imperfections in the words. The field of direct vision may be taken to be that which is focused upon the macula lutea, which is 1.25 mm. in diameter, subtending about 5 degrees of angle at the nodal point.

(*β*) INDIRECT MONOCULAR VISION.—The field of indirect vision ncludes all of the visual field outside of that of direct vision. The figure on next page (Fig. 264) shows the field of indirect vision for white light bounded by the shaded portions of the figure. Note in the centre the 5° circle of direct vision, within which the form and structural features of objects are clearly defined. Note the blind spot (*B*) at the right of the macula in the figure, and showing that the optic nerve enters the eye to the median side of the fovea, located from 12.5° to 17.5° from the centre and a little above the horizontal line from the fovea. Note that the boundary of the field for the indirect vision of the white light crosses the upper vertical meridian at 55°, the median meridian at 60°, the lower vertical meridian at 70°, and the external meridian beyond 90°. The determination of the line bounding the field of vision is called *perimetry;* the record and the nstrument used in getting it, a *perimeter.* The field for yellow light s within that for white, the field for blue light is within that for yellow, the field for red light still farther withdrawn from the periphery, and the field for green very much smaller than that for red. Perimetry has considerable clinical importance because in certain pathologic conditions the perimeters are considerably modified, either by being generally contracted or by being dotted with islands of total or partial blindness.

(γ) Indirect Binocular Vision.—To determine just what the field of indirect binocular vision is, one has only to find the overlapping areas of indirect monocular vision when both eyes are directed to the same point. The accompanying figure (Fig. 264) is for the right eye. If one trace upon the same chart the field sensitive to white light in the left eye, the open external end of the field will extend off to the left and the circular median end to the right, reaching the 60° circle. The right and left perimeters will thus overlap in an almost circular area bounded right and left by the 60° circle, above by the 55° circle, and below by the 70° circle. The field thus bounded is that for binocular indirect vision for white light.

Fig. 264



Perimeter chart with tracings. (Krapart.)

2. VISUAL SENSATIONS.

a. Fundamental Sensations.

The sensations which light induces in the sensorium may not be so easily differentiated as are those of sound, but they are closely analogous to sound. In sound we differentiate pitch, loudness, and quality, dependent respectively upon number of vibrations per unit of time, upon the amplitude of the vibrations, and upon combinaions of overtones; in light we differentiate *color*, *intensity*, and *form*, dependent respectively upon number of vibrations per unit time, upon he amplitude of the vibrations, and upon combinations of intensities lights and shadows).

1. **Form.**—The sensation of detail in structure is clearest at the fovea centralis and decreases progressively in every direction from that point in the retina. That this specialization of form sensation is in some way connected with the fact that, of the rods and cones, cones only are present in the macula, and these are brought into special prominence in the fovea, has been suggested (p. 620); but the color sensation is also induced by stimulation of the fovea, though Kühne and others show that differentiation of color is less acute at the fovea than in the area outside of it.

2. **Intensity.**—Intensity depends upon the amplitude of the vibration of the medium which last transmits the light to the eye. As in the case of intensity of sound, this may depend upon the amplitude of vibration of the sonorous or the luminiferous body, or upon the summation of the effects of several vibrating bodies. The sound produced by two sonorous bodies of the same pitch and amplitude will be more intense because of the summation of the undulations; in the same way the light produced by two candles will be more intense than that produced by one.

The sensation induced by lights of varying intensity is not commensurate with the intensity, but obeys Weber's law of sensation: "The smallest change in the magnitude of a stimulus which one can appreciate through a change in one's sensation always bears the same proportion to the whole magnitude of the stimulus." (As formulated by Foster.) Applied to vision, the proportion is 1 to 100; that is, 0.1 candle power added to or subtracted from a 10-candle-power light, 1 candle added to or subtracted from a 100-candle-power light, and 10 candles in a 1000-candle-power light can be detected, and so on.

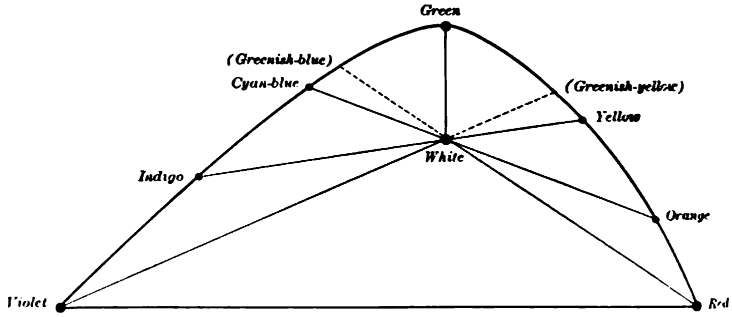
3. **Color.**—Color depends upon the number of vibrations of a luminous body, as pitch depends upon the number of vibrations of a sonorous body. The white light that comes from the sun may be readily decomposed into a number of principal colors and an innumerable number of intermediate mixtures. The principal colors have the following rate of vibration: red, 392 trillions of vibrations per second; orange, 532 trillions; yellow, 563 trillions; green, 607 trillions; blue, 653 trillions; indigo, 676 trillions; violet, 757 trillions. These vibrations range in wave lengths from 766 millionths of a millimetre to about half of that length. The colors named above are the principal or the clearly pronounced colors of the spectrum. From three of these all other colors may be produced; these three are the funda-

mental or *primary colors: red, green, violet.* The accompanying figure (Fig. 265) shows graphically the relation which these colors bear to each other. Not only does a combination of all of the colors produce white, but a combination of certain of the colors in pairs produces white; these pairs are called complementary colors: (I) red and greenish-blue; (II) yellow and indigo; (III) orange and cyan blue; (IV) violet and greenish-yellow.

How the different colors can stimulate the retina has been the subject of considerable controversy.

(*a*) **The Young-Helmholtz Theory** assumes that there are in the retina three different kinds of sensory elements which respond to the three different primary colors—red, green, and violet—and that "*every color of the spectrum excites all of the elements, some of them feebly, others strongly.*" (Landois.) The perception of color is then a resultant of the combined sensations brought to the sensorium by the three sets of elements.

FIG. 265



Geometric color table.

(*b*) **The Hering Theory** is based upon the principles of metabolism and upon the color law of Grassman: "If two simple but non-complementary spectral colors be mixed with each other, they give rise to the color sensation which may be represented by a color lying in the spectrum between both and mixed with a certain quantity of white"—*i. e.*, every color sensation except those of the primary colors may be produced by a color of the spectrum plus white. Hering assumes (I) that light produces metabolism in the retina; (II) that the metabolic processes are in part anabolic and in part katabolic; (III) that white, red, and yellow sensations are katabolic—*i. e.*, accompanied by disintegration and fatigue; and that black, green, and blue sensations are anabolic—*i. e.*, accompanied by integration and rest; (IV) these metabolic processes are assumed to be paired—*i. e.*, white and black sensations affect the same visual substance in opposite directions, red and green stimulate another visual substance, and yellow and blue stimulate a third. Now, according to Grassman's law of color sensation, any color sensation, except that of a primary color, may be produced by a color of the spectrum plus white. Hering assumes that white visual substance is katabolized not only when one sees white, but incidentally in all color sensations except primary ones.

(*c*) **The Franklin Theory** is not antagonistic to either of the foregoing, but rather supplementary. It is based upon the facts of comparative physiology, and assumes that the rudimentary eye distinguishes between light and dark only, and possesses neither form nor color senses; so that the fundamental point of departure is a sensation of simple light or dark (Hering's white and black sensation) produced by stimulation of a fundamental "*visual gray,*" which causes an accentuation of either the white or the black in it (presumably by modifications in the metabolism set up). This theory assumes that the yellow-blue substance was next developed and the red-green last.

The adherents of either the Young-Helmholtz or the Hering theory, especially the latter, may well accept the Franklin theory as supplementary, as it accounts easily for the fact that red-green color-blindness is most common, and yellow-blue blindness rather rare, while inability to see black and white is only found in cases of congenital total blindness. Furthermore, reference to the perimeter chart shows that white-black covers the largest area of the retina, yellow-blue an area within that which red-green is smallest and quite near the centre.

b. Secondary Sensations.

1. **After-images.**—If one fix the gaze upon a brightly illuminated figure or pattern for fifteen seconds and then direct it toward a plain surface, the image of the pattern gazed at will be seen upon the plain background of the second field of vision. If the after-image has the same colors as the first, it is called a *positive after-image.* Positive after-images are usually caused by strong stimuli of short duration rather than by moderate stimuli of long duration. If the after-image is in the complementary color of the original pattern, it is called a *negative after-image.* If one gaze intently at a green pattern, then turn to a red field, the pattern appears deep red upon the red field. It will also appear red upon a neutral field. *Negative after-images are a sign of retinal fatigue.*

2. **Contrast.**—Contrast is the accentuation of a color sensation through contiguity or succession of another color, especially a complementary color. A piece of note-paper may look white upon a black background, but if it is put upon a really white background it will be seen to be far from white. In a similar manner blue or yellow accentuate each other as do red and green. Various other combi-

nations have this reciprocal effect. If the effect is produced by looking at the two contrasting colors at the same time, the sensation is called *simultaneous contrast;* if by looking at the contrasting colors one after another, it is called *successive contrast.*

c. Color-blindness.

Of the male population 4 per cent. or 5 per cent. and of the female population about 1 per cent. are unable to differentiate certain colors. Such persons are called "color-blind."

1. **Complete Color-blindness. Achromatopsy.**—Individuals thus afflicted can distinguish lights and shades, but have no color sense whatever. According to the Hering theory they lack both the red-green and the yellow-blue visual substance; according to the Franklin theory they represent cases of arrested development of color sense in a condition representing a very primitive condition when only the fundamental color substance is present.

2. **Yellow-blue Blindness.**—In this condition the blue end of the spectrum is absolutely dark and the yellow may be more or less *illuminated,* but void of *color.* This represents also an arrest of development; but this arrest occurs after considerable progress has been made.

3. **Red-green Blindness** is by far the most common form of color-blindness. This is assumed by the Franklin theory to represent the last step in the development of the color sense, and, therefore, the first to fail in case of an arrest of development.

4. **Acquired Color-blindness** may result from disease of the retina.

5. **Normal Color-blindness** exists in the periphery of the retina. Passing from without inward the outermost sensation is that of white (and black); the next that of yellow and blue, followed by red and green. (See Perimetry.)

3. VISUAL PERCEPTIONS AND JUDGMENTS.

One may have a sensation of black lines upon a white surface without perceiving in the lines a letter or word. The retinocerebral apparatus brings to the sensorium of the untutored savage the same sensations as it does to the sensorium of the scholar. The savage "senses" a written word upon a page, but does not *perceive* it; on the other hand, the scholar may "sense" the twigs upon the forest path without perceiving in their position and condition the track of an animal. Simple sensation involves nothing higher than the sensorium. There is no reason to believe that the sensorium brings to the consciousness of different individuals different sensations. Perception involves cerebration in the interpretation of sensations.

erception involves previous knowledge or memory of the same or elated sensations. Effectual perception, like effectual marksmanship, epends upon the man behind the instrument.

Visual perception is the *seeing with understanding*. *Visual judg-ents* are based upon visual perceptions and represent conclusions eached after comparison of previous perceptions.

a. Acuteness of Vision.

It is frequently necessary to test the acuteness of vision through comparison of visual perceptions. An individual whose acuteness f vision is in question presents himself to the ophthalmologist for xamination. If the subject is schooled in interpreting dim and istorted images he may mislead the observer for a few moments ith his acute perception, but the faulty sensation must, sooner or ater, reveal itself. The observer will present to the subject a eries of letters in unusual combinations, so that there will be no ay in which he can get a clue for his judgment to work upon.

To be more concrete: The acuteness of vision is tested by reading etters of various heights at various distances. The normal eye emmetropic eye) should see clearly at 6 m.—the oculist's infinity—etters which subtend an angle of 5′—*i. e.*, letters 1⅛ cm. in height. t 12 m. the normal eye should distinguish and name letters hich are 2¼ cm. in height. These letters subtend an angle of 5′—he minimum angle of clear vision. If the individual can see at 6 m. nly what he should see at 12 m., he is credited with Vision = $\frac{6}{12}$. f he can see at 6 m. what he should see at 30 m., he is credited with Vision = $\frac{6}{30}$. If by cultivation the visual power has been brought p above the average, so that he can see at 6 m. what the average ye must bring to 3 m. to see, he will be credited with Vision = $\frac{6}{3}$.

The acuteness of vision varies much with the habits and employ-ent of the individual. Persons employed at fine, close work acquire microscopic vision—*i. e.*, ability to see and interpret the minutest etail of structure. Watchmakers and jewellers acquire this ability. Persons employed in vocations which require long-distance vision cquire telescopic eyes—*i. e.*, ability to see and interpret structure f distant objects. Sailors and rangemen possess this ability to a arked degree.

b. Visual Estimates.

1. **Estimate of Distance.**—This judgment is based upon a ombination of at least two sensations or perceptions: (1) sensation f the accommodation required to focus the image of the object

upon the retina; (II) the sensation of the convergence required to direct the two visual lines at the same object in the binocular vision. These sensations are examples of muscular sense. One estimates these muscular efforts instinctively. Upon these instinctive estimates one bases his judgment of the distance of an object. But other considerations may enter in to assist in the estimate of distance. For example, a movement of the head or body causes a displacement of nearer objects in the background formed by more distinct objects; one learns by experience how much this displacement should be for given distances and bases his judgment accordingly. The known size of an object is an important factor in the estimate of its distance. In this estimate one instinctively measures the image and compares it with the image of the same object at a short distance.

2. **Estimate of Size**—This judgment is based upon two perceptions: (I) the size of the image, and (II) the distance of the object. Various other considerations may enter in to modify the judgment.

The subject of visual illusions belongs more properly to psychology than to physiology, and will, therefore, not be discussed here.

CHAPTER XI.

THE PHYSIOLOGY OF THE NERVOUS SYSTEM.

. THE NEURONE: STRUCTURAL AND FUNCTIONAL UNIT OF THE NERVOUS SYSTEM.

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    - (2) The Dendrites.
    - (3) The Axone.
    - (4) The Collaterals.
- *b*. Origin of Neurones.
- *c*. Types of Neurones.
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- *e*. The Neuronal Theory.

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    - (1) Wallerian Degeneration.
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        - (*a*) *The End Organ Theory.*
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- *f*. The Inhibitory Power of Neurones.
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- (2) THE COURSE TAKEN BY TACTILE IMPULSES.
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- (2) THE COURSE TAKEN BY CO-ORDINATING IMPULSES FROM THE CEREBELLUM.

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- (3) MECHANICAL CHARACTER OF REFLEX ACTION.
- (4) SUMMATION OF STIMULI.
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  - *Pathologic Reflexes.*
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  - *IV. The Circulatory Reflex.*
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3. PATHOLOGIC PHYSIOLOGY OF THE CEREBRAL CORTEX.
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4. THE FUNCTION OF THE CORPUS CALLOSUM.
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6. THE FUNCTION OF THE INTERNAL CAPSULE.
7. HIGHER CEREBRAL FUNCTIONS.

THE PHYSIOLOGY OF THE NERVOUS SYSTEM.[1]

A. THE NEURONE: STRUCTURAL AND FUNCTIONAL UNIT OF THE NERVOUS SYSTEM.

1. THE STRUCTURE OF THE NEURONE.

In the study of the physiology of the nervous system, a definite comprehension of the neurone is the first requisite. The older conception of the nervous system as functioning according to its large anatomic divisions has gradually given place to that which recognizes the nerve cell and its processes as the unit of nerve function. This unit is the neurone.

a. General Description.

The term *Neurone* signifies a nerve cell with all of its processes. Waldeyer first used the term in 1891.[2] Neurones, constituting as they do single body cells, like liver cells or muscle cells, possess certain general cell characteristics, such as protoplasm, limiting membrane, nucleus, and nucleolus. Indeed, within the last few years there have been found in many of the adult nerve cells formerly supposed to be incapable of indirect cellular division a centrosome and an attraction sphere, thus bringing them nearer the type cell. The distinguishing feature of the nerve cell, however, is its possession of a large number of fibrous prolongations from the cell body, these processes frequently constituting a maze of feltwork almost impossible to unravel. One of these processes, more distinct than the others, seldom branches and preserves a fairly uniform calibre and appearance; this is the *axone*. If it has branches they are usually single ones and are called *collaterals*. The remaining processes of the cells, distinctly protoplasmic outgrowths, branch dichotomously much as do the branches of trees; for them His proposed the term *dendrites*, a name which has received universal recognition.

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[1] For a general introduction the student is referred to the chapter on General Physiology, p. 96 *et seq*. It is assumed that a study of the gross anatomy of the nervous system has been made, and, therefore, to the largest extent possible it will be sought to avoid entering that field here.

[2] Deutsche medicinische Wochenschrift, 1891.

1. **The Neuronal Cell Body.**—The cell body is of varying sizes and shapes in different portions of the nervous system. In the ganglia of the posterior spinal roots unipolar cells are found; in the cortex of the brain there are bipolar cells, and in various parts of the nervous system multipolar cells, as in the motor centres of the cerebral cortex and in the ventral horns of the spinal cord. The cell bodies vary in size from four to one hundred and thirty-five or more micromillimetres in diameter. Among the very large cells are the motor cells of the ventral horn and the cells of Clarke's vesicular column in the spinal cord, Purkinje's cells in the cerebellum, and the large pyramidal cells of the cerebral cortex. Among the smaller cells are those of Waldeyer's central cell column and those of the substantia gelatinosa Rolandi in the spinal cord, the granular cells of the cortex of the cerebellum and cerebrum, and the cells of the bulbus olfactorius. Some of the cells may be so large as to be seen with the naked eye, particularly the cells of Purkinje.

Not all nerve cells possess a *limiting membrane* or capsule. Such a membrane is possessed by the cells of the dorsal spinal ganglion and the sympathetic ganglionic cells, but is absent in the case of the large motor cells of the ventral horn of the spinal cord. The *protoplasm* can be roughly divided into a peripheral exoplasmic portion and a central endoplasmic part. The cytoplasm throughout presents a delicate fibrillated structure, the fibrillæ being still the subject of much controversy. In addition to the intracellular fibrillæ there were discovered and described by Nissl, in 1885, what have since been almost universally known as *Nissl's bodies*, though von Lenhossék has proposed for them the term *tigroid bodies*. These masses, best understood by a reference to Figs. 266, 267 and 268, are made the basis of an elaborate classification by Nissl, his arkyochrome cells being those in which the tigroid bodies are arranged in the form of a network, while his stichochrome cells are those in which the tigroid bodies are arranged as stripes or lines, parallel either with the cell wall or the nucleus. His gryochrome cells are those in which the stainable parts of the cytoplasm are made up wholly of small granules.

The nature of the tigroid masses is a matter of controversy; at all events they are basophilic as regards staining properties. Studied in very thin sections, one-half to one micron in thickness after Held's method, they are found with high powers to be made up of a mixture of very small and of somewhat coarser granules, of rounded form, arranged in rows and radii, and apparently buried in a coagulum-like matrix. The tigroid masses are invisible in fresh cells and are

Fig. 266

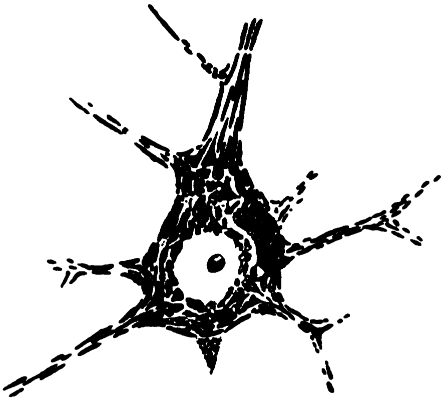


Fig. 267

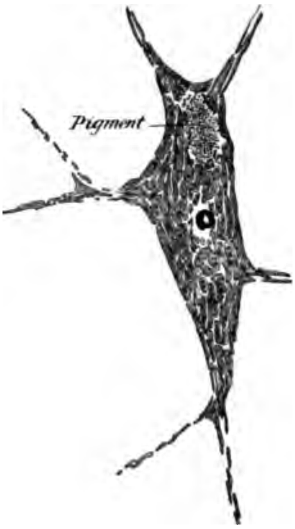
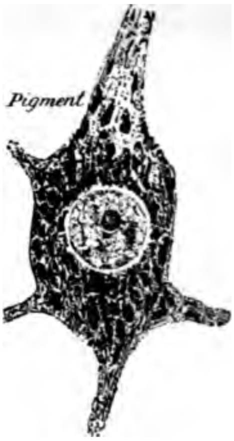


Fig. 268



Typical cell bodies from the central nervous system. (After Edinger.)

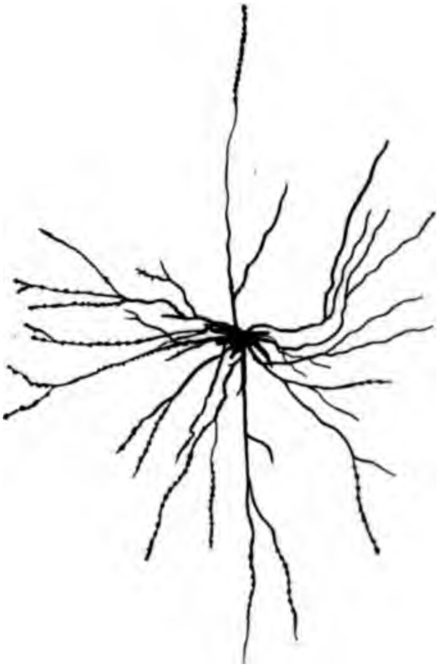
ently precipitates due to the Nissl method of fixation and ıg. They resist digestion with pepsin and hydrochloric acid ly temperatures, as has been determined by Held. They are ısoluble in acetic acid, ether, and chloroform, but, on the other are easily dissolved by alkalies, particularly carbonate of n. They give positive results when tested with phosphorus egative ones when tested for iron.[1] Held regards the bodies onging to the nucleoalbumins, and this view is doubtless t.

ween Nissl's bodies lies the unstainable portion of the cyto-, and the quantitative relations of the former to the latter vary ously. Thus in the cells of the ventral horn of the cord the ble substance of Nissl preponderates, whereas in the cells of ıje the unstainable substance greatly exceeds the stainable. ling to Rosin, the unble substance is acido- and in it, according to r, Apáthy, and Bethe, ımerous nerve fibrils. der to demonstrate fibrils it is first neces- ɔ dissolve the tigroid with ammonium. The ıtion is then found to re pronounced in the eral exoplasmic por- f the nerve cell than endoplasm.

ides Nissl's bodies and nstainable fibrillated n of the protoplasm, of the larger nerve ossess a mass of pig- d matter, in addition ther large nucleus with nct nucleolus.

he Dendrites.—The lasmic processes called ites (see Figs. 269, 270 271) resemble more in appearance and bility the cell body itself than does the axone. They leave the asm by broad, thick bases, and divide and subdivide into

FIG. 269



A typical neurone, showing dendrites, bearing gemmules. (After Kölliker.)

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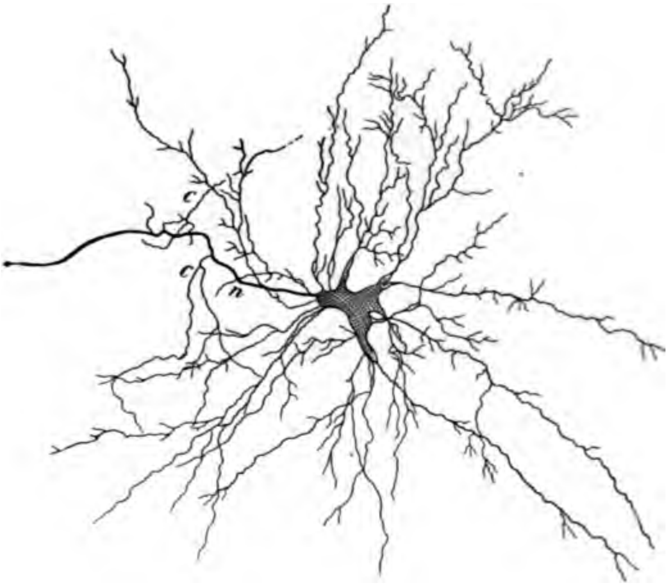
[1] llum, British Medical Journal, 1898, vol. ii. p. 778. Macallum, in this paper, claims to monstrated the presence of iron.

numerous fine twigs which end in free extremities. The dendrites of a given cell, as well as those of different cells, vary enormously in length and numbers. In some cells one dendrite may be greatly developed, while the others remain small and slender. The dendrites are seldom straight in their course, and are usually irregular in contour, in marked contrast to the axones. The branching of a dendrite may occur near to or at some distance from its origin at the cell body, and these branches almost never anastomose with one another. They merely touch each other, thus producing a feltwork in contradistinction to a network.

FIG. 270

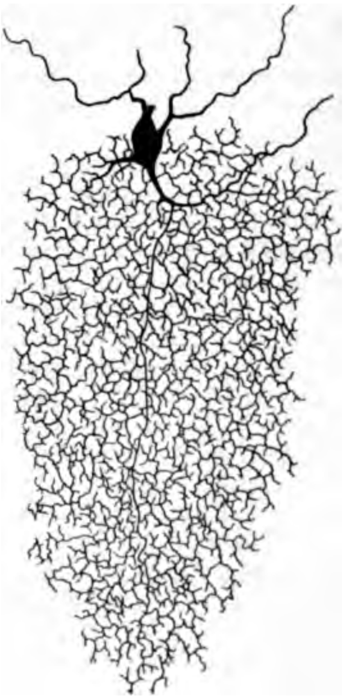


Golgi's cell, type I. Cell from the optic tract of the cat laterally from the lateral geniculate body. Radiating from the cell body are to be seen very many protoplasmic processes which show a broad wedge of origin and branch characteristically; the single axis cylinder process, or axone, *n*, has a smooth surface and tolerably even calibre, which is maintained for a considerable distance from the cell. It gives off a few delicate lateral branches or collaterals, *c*. (After Kölliker.)

In some cells the dendritic tufts cover a surprisingly large area; in others they are relatively insignificant in extent. Again, from some cell bodies the dendrites originate apparently from nearly every point of the cell surface, whereas in others a more or less considerable portion of this surface is smooth and unbroken. Some cells, indeed, are wholly destitute of dendrites, and are hence called adendritic; but some of these cells possess axones from which there issue non-medullated branches dividing in a manner characteristic of dendrites and termed axodendrites by von Lenhossék. The unipolar cells of he dorsal spinal ganglia apparently are without dendrites, but tudied embryologically they are found to be primarily bipolar, in which condition they always remain in the case of the ganglia of the ighth cranial nerve. In the adult cell the single dendrite stretching between periphery and ganglion is anatomically an axone, but mbryologically and physiologically t is a dendrite, as was first pointed out by Ramón y Cajal in 1889.

In general, dendrites are destitute of a myelin sheath, whereas axones possess them. The posterior spinal ganglion cell affords an exception o the rule, its single dendrite being medullated and accurately simuating a dendrite.

FIG. 271



Golgi's cell, type II. Nerve-cell with short branched axis cylinder, or axone, from the granular layer of the cerebellum of a cat aged eight days. (After Van Gehuchten.)

The dendrites of many nerve cells are characterized by enlargements along their course, first described by Berkley, of Baltimore, in 1896, and to which he gave the name *gemmules*. (See Fig. 269.) At one ime they were supposed to arise rom artificial causes, such as fixaion and staining by silver nitrate, but so constant is their presence n certain cortical cells, and so constant is their absence in others, that hey are generally regarded as real and not artificial. They appear uniformly and most clearly on the dendrites of the pyramidal cells of Betz and the cells of Purkinje fixed and stained by the Golgi method. Berkley suggests that by increasing the surface of the dendrites they increase the number of contact points. Their absence from the pyramidal cells in cases of cortical atrophy, as in general paralysis of the insane, is very suggestive.

3. **The Axone.**—Axones differ from dendrites in several respects: (I) They leave their respective cell bodies by narrow, wedge-shaped beginnings, as contrasted with the dendrites which have broad protoplasmic trunks. The origin of the axone is called the *axone hillock*, and is destitute of Nissl's bodies, though it shows distinctly a fine fibrillation continuous with that of the cell body. (II) The dark bodies of Nissl, found in the cell body and its dendrites, are not found in the axone. (III) The calibre of the axone varies less with its

length than does that of the dendrites from the same cell, and it is usually maintained for some distance. (IV) The surface of the axone is smooth, its walls being parallel, whereas the surface of the dendrite is very uneven, frequently being made so by the presence of gemmules. (V) The axone, as a rule, pursues a direct course from origin to destination and is not branched (though it may possess collaterals), whereas the pathway of the dendrites is a devious one, and it branches diffusely. (VI) The bulk of all the dendrites of a given cell is usually less than the bulk of the cell body, whereas the bulk of the axone, by reason of its great length, may be 220 times greater than the bulk of the cell body from which it springs. (Donaldson.)

The length of an axone varies from a few millimetres to half the height of an individual. The longest ones, called inaxones by von Lenhossék, are those of the motor paths from brain into cord, or from cord to muscles. Most neurones are *monaxonic*, in that they possess but one axone; but some are *diaxonic*, and some are *polyaxonic*. The dorsal spinal ganglion cell is often called diaxonic, because that portion of the cell entering the cord and that portion extending to the periphery are structurally axones, although, as we have seen, the latter process is embryologically and functionally a dendrite. An axone which branches by a T-shaped division, as those entering the column of Burdach from the dorsal spinal ganglion cell, is called a *schizaxone*. Polyaxonic cells are rare; Ramón y Cajal has found them in the sympathetic system, notably in Auerbach's and Meissner's plexuses. Neurones without axones, found, for example, in the bulbus olfactorius, retina, and in the basket cells about the cells of Purkinje, are called *anaxonic* cells.

The distal ends of axones are usually branched and free. The branches may form an arborization around either a single cell or a dendrite, though the actual demonstration of such arborization is very rare. It is, however, very convenient for diagrammatic purposes to represent in most instances the arborization between the end of an axone and the beginning of a dendrite, but the student is warned that such representations are almost invariably purely diagrammatic. Many curious forms of termination besides arborization occur, among them being the "climbing fibres" of the cerebellar cortex, the "disks" of Meissner's corpuscles, and the motor plates at the end of the motor axones.

Axones are usually, but not invariably, medullated. External to the myelin sheath is the neurilemma, which is always wanting, however, in the cerebrospinal axis. The axones in the sympathetic system are non-medullated, but they possess a neurilemma. The medullary sheath, when present, is usually wanting near the cell body, and is absent at the end of the axone, as, for example, about the terminal motor plates.

4. **Collaterals.**—The collateral branches of an axone are divided by von Lenhossék into two groups: the axodendrites, which are non-medullated, and the paraxones, which possess a medullary sheath f the axone itself possesses one. This distinction is a good one, hough the terms themselves may be dispensed with in the interest of simplicity. The collaterals leave the axone by wedge-shaped buddings, almost at right angles to it. They usually make their way o the dendrites or cell bodies of other neurones, about which they orm arborizations, and so establish new and manifold relations. Thus complicated reflexes are easily explained by the intervention of collaterals, and thus also is explained Ramón y Cajal's term of *avalanche conduction*, since the axone of one neurone may send mpulses through its collaterals to many neurones, and each one of hese to many more in turn. Though the number of collaterals which an axone may possess has never been determined, Kölliker was fortunate enough to find nine issuing from an axone followed for a few millimetres in a longitudinal section of the cord. Some axones possess no collaterals, as those emerging from the motor cells n the ventral horn of the spinal cord. In general it may be affirmed hat those axones which course through the cerebrospinal axis are provided with collaterals, while those in the peripheral nervous system are devoid of them; and when they are present, they are more numerous along that part of the axone near the cell body (cytoproximal end) than beyond in the cytodistal portion. This would ead one to suppose that in the spinal cord more collaterals are to be found in the column of Burdach than in the column of Goll, which s true; the latter fasciculus, made up of the cytodistal portions of axones which lower down in the cord occupy the column of Burdach, s practically free from collaterals.

b. Origin of Neurones.

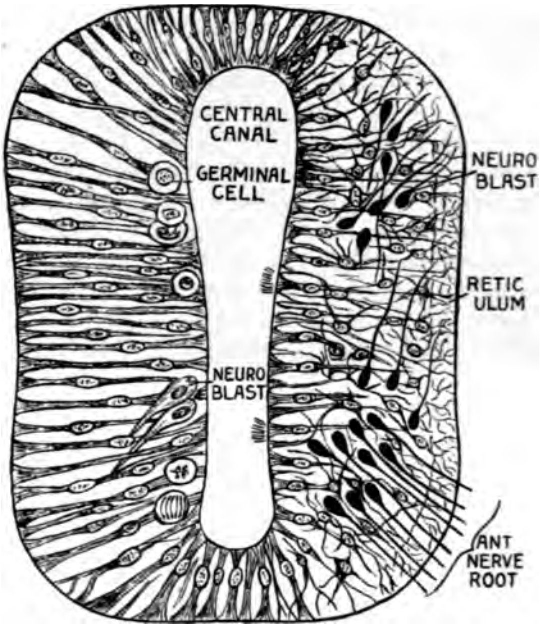
In the earliest stages of embryonic life the cerebrospinal axis consists simply of a thin-walled tube, formed by a single layer of columnar epithelium derived from the ectoderm. (See Fig. 272.) Subsequently, according to His, large round cells, called by him *germinal cells*, begin to appear in the intervals between the columnar cells; and about the fourth week of embryonic life they form an almost continuous layer. At this stage these cells have no processes; so that although there is a nervous system, as His remarks, there are no nerves. Later these germinal cells begin to migrate to the peripheral portion of the neural tube, become pyriform in shape, and are known as *neuroblasts*. The stalk of the cell directed away from the ectodermic surface becomes the axone, and from the opposite pole the dendrites begin to develop. Thus both axone and dendrites are derivations of the cell body. The original columnar cells become the ependymal cells, or develop into the neuroglia cells which serve as a supporting framework.

c. Types of Neurones.

Depending upon the anatomic appearance of the axone, Golgi distinguished two types of neurones which are generally spoken of as Golgi's "cell type I and cell type II."

(*a*) **The Cell Type I,** illustrated in Fig. 270, shows an axone which fails to branch, which stands out as a distinct fibre, of the same average calibre throughout, with smooth parallel walls. It was Golgi's idea that such cells were motor, since motor cells in general belonged to this type. The distal end of such an axone usually breaks up into an arborization, the single branches of which are in a relation of contiguity with the dendrites of another neurone or its cell body, or, as in the case of a peripheral motor neurone, are flattened out on the muscle fibres, forming the motor end-plates of the nerve.

Fig. 272



Transverse section through the early neural tube. Diagrammatic. The left side of the section exhibits an earlier stage of development than the right side. (After Alfred H. Young.)

(*b*) **Golgi's Cell Type II** differs from cell type I characteristically only in the branching of the axone, which, by reason of the branching, is sometimes called a *dendraxone.* (See Fig. 271.) In a cell of this type the axone begins to divide very soon after its exit from the cell body into a large number of minute branches forming a dense feltwork in which the axone quickly loses its identity. Golgi's hypothesis that cells of this type are sensory has been swept away by Ramón y Cajal, who has showed that Golgi's cell type I differs from cell type II only in the destination of its respective axone, that of the former ending in an arborization at a considerable distance from the cell body, while that of the latter divides up near the cell body, each being peculiarly adapted to the function required of it. In this way is explained the more frequent occurrence of cells of type I in paths uniting distant portions of gray matter, and the more frequent occurrence of cells of type II in paths uniting adjacent portions of gray matter.

d. Interrelation of Neurones.

A point of great importance with reference to both the physiology and the pathology of the nervous system is the independence of each individual neurone as regards all other neurones histologically. His, in 1881, and Forel, in 1887, were the first to enunciate this doctrine. It had been previously held, owing to the pernicious teachings of Gerlach concerning his alleged network, that the branching processes of neighboring neurones completely anastomosed. But His, from embryologic studies, and Forel, from studies in pathology, stated the principle of contiguity as explaining the interrelations of neurones. Ehrlich's method of staining by methylene blue, either *intra vitam* or *post-mortem* have led to confirmatory results. The late work of Held, Apáthy, Bethe and Nissl has led these observers and their followers to question the absolute individuality of every neurone, for apparently protoplasmic continuity has been established between adjacent neurones. The word apparently is used advisedly, for Ramón y Cajal's latest method of staining (1904), being practically the application of the principles of photographic printing and developing to tissues, has led to results amply confirming his earlier studies. Ramón y Cajal stands to-day the foremost champion of individuality among neurones. Held's doctrine of concrescence between the axone of one neurone and the cell body of another, even though the concrescence in the adult cell leads to complete fusion, does not really impair the doctrine of individuality. The question as to the existence of Apáthy's neurofibrils, so much like the old stumbling-block of Gerlach's nerve network, must be passed by unmentioned.

The teachings of botanists of protoplasmic contiguity among plant cells affords some basis of argument by analogy. But should such contiguity ever be proved, it is difficult to see how it can invalidate individuality among neurones.

e. The Neuronal Theory.

The neuronal theory considers the nervous system, aside from its neuroglia, bloodvessels, and lymphatics, as made up of countless individual nerve elements or neurones. Each of these is a complete autonomous cell, and throughout life it is morphologically and in a sense also physiologically independent of every other neurone, establishing communication with other neurones only by contiguity, as the leaves of two trees may touch, without substance actually passing between them. The axone found in the peripheral nerve, like the protoplasmic process (dendrite) found in the gray matter, forms an integral part of the nerve unit, with organic connection with the cell body, which serves as their trophic and control centre. In higher animals the conduction of nervous impulses usually proceeds in one direction along several neurones, arranged in tandem or in chains, each unit of the chain being in a position to be affected by and in turn to affect one or several other neurones. Thus tracts are made and pathways of association, and thus distant sense organs and muscles are brought into relation with the cerebrospinal centre. To end by a quotation from Barker's excellent treatise on the neurone: "The nerve life of the individual, including all his reflex, instinctive and volitional activities, is the sum total of the life of his mill'ard of neurones."

2. THE PHYSIOLOGY OF THE NEURONE.

a. Effect of Mutilation upon the Neurone.

1. **Wallerian Degeneration.**—When a peripheral nerve is severed the distal portion degenerates; the myelin sheath is broken up and absorbed, the axone itself dissolves and disappears, and even the neurilemma ultimately shows alteration. The process is called *Wallerian degeneration*, after Waller, who first thoroughly studied and described it (1850). Sometimes it is called *descending degeneration*, not because it begins at the point severed and proceeds distally, for, on the contrary, the whole distal segment degenerates simultaneously throughout its length, but because it follows down the course of the nerve fibre. Waller proved that such degeneration took place in the distal segments of both motor and sensory fibres. Moreover, he proved that if the sensory root were severed between the dorsal spinal ganglion and the spinal cord the degeneration followed in certain fibres located in the columns of Burdach and Goll. The interpretation of these facts did not follow until more than thirty years later, when His demonstrated that the peripheral nerves contained processes directly connected with nerve cells, either in the

ventral horn of the spinal cord or in the dorsal spinal ganglion; and that the fibres of the columns of Goll and Burdach are the axones of the cells of the dorsal ganglion. Stated in a more modern way Waller's law is as follows: Whenever an axone is severed from the cell body from which it issues, the portion distal to the point severed degenerates. This degeneration involves not only the axone, but also its main terminals, its collaterals, and their terminals.

The value of the application of Waller's law properly interpreted has been immense. If the trophic centre—that is, the cell body of a given fibre—is to be determined, section with study of the ensuing degeneration affords the solution. Thus, in a transverse section of the spinal cord, strands of degeneration found *above* the lesion demonstrate that the cell bodies of the degenerated fibres lie below it; whereas, strands of degeneration found *below* the lesion demonstrate that the cell bodies or trophic centres lie above it. Thus Türck discovered the course and direction of the pyramidal tract fibres, and since his discovery (1852) immense progress has been made by this method in unravelling the complicated relations of the fibres and tracts in the cerebrospinal axis.

2. **Retrograde Degeneration.**—Another form of degeneration has been called *retrograde degeneration* by Nissl, a degeneration which, after division of an axone, involves both the proximal portion of the severed fibre and its cell body. Shortly after Waller's study and the enunciation of the law bearing his name, it was found that after amputation of a limb the motor fibres proximally located slowly wasted and disappeared. This was directly contrary to Waller's teachings, for he insisted that the proximal portion remained in a state of integrity, the distal portion alone degenerating. Marinesco, in 1892, showed that not only do the proximal fibres disappear after amputation of a limb, but that the gray matter of the spinal cord also disappears in part. Thus the whole neurone is lost. More valuable is Nissl's recent study. Nissl has actually demonstrated that shortly after an axone is severed from the cell body rarefaction and granulation of the Nissl bodies follow, and his observations have been confirmed by other observers (Flatau). Thus it results that when an axone is severed *the whole neurone suffers*, and, the nearer the point of injury of the axone is to the cell body, the greater the effect upon the neurone as a whole. Although it has not hitherto been possible to study dendrites as accurately as it has been to study axones, it is undoubtedly true that injuries to them are also followed by changes within the cell body.

3. **Injury to Cell Body.**—When the cell body is directly interfered with, death of the axone and dendrites follows. For example, if the abdominal aorta of a rabbit be ligatured for thirty minutes or an hour, there results permanent sensory and motor paralysis of the posterior extremities because of necrosis of the cells in the spinal cord. Subse-

quent histologic study shows complete degeneration of the entire neurone and is easily made out within a very few days by the application of the Marchi method. Poisons circulating in the blood produce similar effects upon the neurone.

4. **The Conclusion** of the whole matter of mutilation of a neurone is this: *Injury to any part of a neurone affects more or less all other parts. The neurone as a whole, therefore, is a trophic unit, and the exact location of the trophic function in any particular part of it is not yet established, though it seems not unlikely that trophic impulses proceed from the cell body into its processes.*

b. The Activity of the Neurone.

Neurones are unremitting in their activities. Like all living matter, they know no repose. Impulses are constantly passing to the cerebrospinal centres in control of our physical processes, yet we are wholly unconscious of them. Similarly impulses are passing continuously to our muscles, insufficient to cause muscular contractions, but sufficient to preserve their tonus and nutrition, and of these we are not conscious. The nature of this activity is, however, unknown, even after half a century of arduous investigation by physiologists. Undoubtedly the vital manifestations are vested in the metabolic activities of the cell body, but the chemistry of the nerve cells is far beyond our present knowledge. The importance of normal impulses, both efferent and afferent, for the welfare of the neurone is, however, certain. Without such impulses, received or emitted, there can be no life; the cell atrophies because it is unused.

Is there such a thing as automatic or *spontaneous activity* in neurones? "If among external stimuli we class not simply those outside the body, in which event a very minute fraction of the whole number of neurones would be directly accessible to external stimuli, but all those external to a given neurone, including those arriving through the lymph which bathes it, or by means of the processes of other neurones which enter into relations of conduction with it, we shall come to the conclusion that the limits of genuine spontaneity of action on the part of neurones are very narrow; indeed, some authors would deny its existence altogether."[1] Von Lenhossék, for example, regards the question as finally settled, and boldly affirms that there is no nerve cell which of itself alone is active; external stimuli invariably are the incitants of its activities. Indeed, reflex actions are by definition the result of external stimuli, and even volitional movements are reflex actions modified by memories. And memories themselves are but recollections invariably awakened through the law of association of ideas by external causes.

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[1] L. F. Barker, The Nervous System, p. 252.

c. The Effect of Activity upon the Neurone.

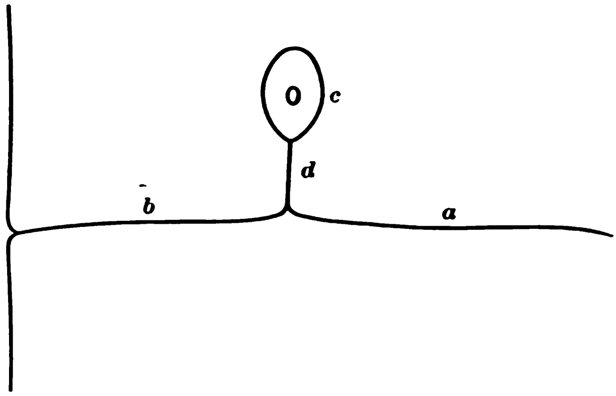
ıough the neurone is incessantly active, activity is a relative
, and there are various degrees of it. Very slight activity is
ally repose, and during repose the anabolic processes in the
: cell are doubtless in the ascendancy. Lugaro finds that during
:rate activity the protoplasm becomes somewhat turgescent, and
the nucleus undergoes no change in size. In the earlier phases
:tivity the stainable substance of Nissl apparently increases in
ınt, but subsequently it is diminished. Hodge, who is the
:er in the subject of the effect of fatigue upon nerve cells, has
ed the protoplasm and nucleus after five hours of faradization,
found that the fatigued cell was decreased in size, that the
:us was shrunken, showing zigzag borders and staining more
ly than the normal, and that the protoplasm was often shrunken
stained faintly. These alterations, also observed in nerve cells
ıney-bees, swallows, and pigeons after a day of flight, disappeared
ıg a night's rest. This recuperative ability is sometimes lost,
a condition of pathologic physiology results. The condition
rn as neurasthenia apparently has for its basis an inability on
ɔart of the neurone to recover from fatigue. Based upon this
ral inability is the Edinger-Weigert *Ersatz Theorie* of locomotor
a, and based upon it, furthermore, is the Weir Mitchell rest
with forced feeding.

d. Function of the Dendrites.

l anatomists and physiologists are agreed that the axone has
unction of conduction of impulses; but concerning the function
ınduction in dendrites there has been much dispute. Even the
body itself has been regarded as unnecessary for conduction,
ment being based upon the dorsal spinal ganglion cell, unipolar
pe, the impulses being supposed to pass directly from the dendrite
ı the axone (II), and the cell body (III), the short arm (IV) being
:ded as taking no part in conduction. (See Fig. 273). This idea
disproved by Wundt (1871–1876), who demonstrated that there
:lelay of 0.003 of a second in the passage of an impulse through
lorsal spinal ganglion, this time being consumed by the passage
e impulse through *b* to the cell body (*d*) and back again through
c. Moreover, the development of the dorsal spinal ganglion
in lower animals shows it to be originally bipolar, so that the
ılse is forced to enter the cell on one side and to emerge from
ther. Thus the dorsal spinal ganglion cell *is a physiologic unit*,
r part of it being used in conduction, both dendrite, cell body,
axone; and what is true of this neurone is true probably of all
ɔnes.

It is to be admitted, however, that some anatomists and physiologists assume a different function for dendrites. Instead of regarding them as the equivalents of the branches of a tree, Golgi and his followers have looked upon them as the equivalents of roots sucking nutriment from the adjacent blood or lymphatic vessels, and supplying it to the cell body. In support of this theory are some instances of apparently direct attachment of the ends of dendrites to bloodvessel walls; but while such isolated instances undoubtedly exist, no such arrangement exists uniformly for all dendrites. Again, the Golgi school draws attention to the masses of dendrites directed toward the cortical surface of cerebrum and cerebellum, the inference being that nutriment is drawn by them from the bloodvessels of the pia. Von Kölliker, who has reviewed this question, concluded that while the balance inclines toward the nervous nature of dendrites, there may be some which have no such function, and which may serve only in aiding the nutrition of the cell.

FIG. 273



Diagrammatic. Posterior spinal ganglion cell: *a*, dendrite; *b*, axone; *c*, cell body; *d*, both axone and dendrite.

The most convincing evidence in favor of the nerve function of dendrites is found in the olfactory glomeruli. Ramón y Cajal, an ardent supporter of the function of conduction in dendrites, has shown that the only possible path for the impulses of smell is from the terminals of the olfactory fibrils upward in the glomeruli to the dendrites of the mitral cells. These dendrites, then, conduct the impulse to the cell body, whence it proceeds along the axone, lying in the olfactory tract. Here, then, is one case where the nerve function of conduction in dendrites is definitely proved. Von Kölliker, who has verified Ramón y Cajal's studies, calls attention to the important conclusion, later to be reverted to, that an impulse may pass from one neurone to the fibre of another.

e. Function of the Axone.

Concerning the function of the axone, there has never been anything but unanimity among both anatomists and physiologists; it is universally believed to be a conducting organ. Histologically two sorts of axones are distinguished: (*a*) those which are surrounded by a medullary sheath, and (*b*) those which are devoid of such covering. If an axone is medullated its collaterals are also medullated as far as their terminals. The physiologic importance of this sheath is not well understood. It has been regarded as an insulating substance, thus implying that the impulse passing through the axone is like an electric current passing through an insulated copper wire. In support of this view is the fact elaborated by Flechsig that axones do not acquire their medullary sheaths until they are sufficiently developed to be physiologically active. It is generally believed, therefore, since the myelin is an insulating substance, that there can be no transference of an impulse from one neurone to another except in those parts in which the myelin sheath is absent, and this in the case of medullated axones is only at their terminals or at the terminals of their collaterals. The naked side fibrils of Golgi, or the so-called axodendrites of von Lenhossék (see p. 649), afford unusual opportunities for the transference of impulses from one neurone to another.

On the other hand, the existence of unsheathed nerve fibrils tends to disprove this insulation hypothesis. Certain cranial nerves, such as the olfactory and certain fibres of the pneumogastric nerve, as well as those fibres belonging to the sympathetic system, are either devoid of such a sheath or have only rudimentary ones. The old physiologic rule, that in general those *efferent* fibres which arise from centres in the cerebrospinal axis that are not under voluntary control are naked, still holds good.

1. **Transmission of Impulses.** (*a*) **Direction of Conduction; Cellulipetal and Cellulifugal Messages.**—"The hypothesis that in the neurone the dendrites represent the apparatus for receiving nerve impulses, conducting always in the direction of the cell body (*cellulipetal conduction*), the axones being the discharging processes, conducting always in a direction away from the cell body (*cellulifugal conduction*),"[1] was first advanced by von Gehuchten in 1891. It has been ably advocated by Ramón y Cajal, supported by Retzius, and adopted by von Kölliker, Waldeyer, von Lenhossék, and all leading clinical neurologists. Indeed, it may at the present day be looked upon as one of the fundamental laws of the nervous system, despite the fact that it is not absolutely or incontrovertibly proved for all neurones, though, as was mentioned, it has been proved in the olfactory apparatus.

Are there exceptions to the law above enunciated? Apparently there are. Thus, for example, in cells of Golgi's type II (see Fig. 271), it is obvious that impulses from some of the dendrites must make their way into the cell body partly through the basal portion of the axone. Yet there is nothing to prevent the adoption of the view that such an axone is a compound affair, consisting of a dendritic portion and an axonic portion, and thus the law of conduction is sustained. Von Lenhossék would get around the difficulty by describing the direction of conduction in such dendrites as *axopetal* (seeking the axone), instead of cellulipetal. Another apparent exception is the anaxonic cell. How can it emit impulses if it has no axone? Presumably only by means of the body wall. Diaxonic cells, like those of the dorsal spinal ganglia, are apparent exceptions, but Ramón y Cajal's view, that the peripherally located anatomic axone is physiologically and embryologically a dendrite, has met with very general approval. Von Bechterew is of the opinion that *dendrites conduct both ways*, one neurone transferring its impulses to another by means of interwoven dendrites. This hypothesis is based upon the intimate relations of certain dendrites of the two halves of the cord in the ventral commissure, and upon the relation of the anaxonic cells in the olfactory lobe with the mitral cells.

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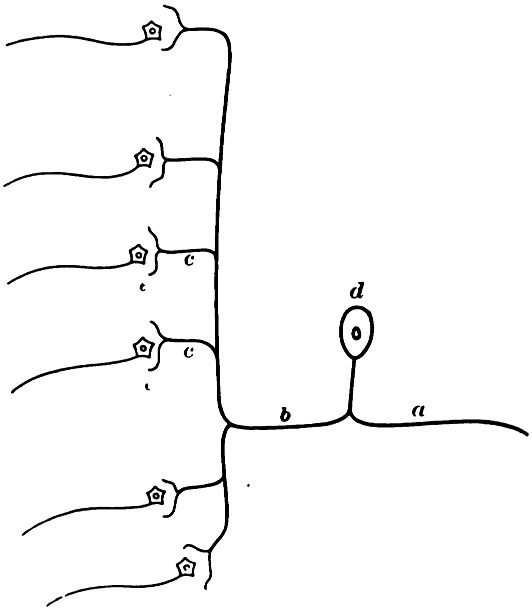
[1] L. F. Barker, loc. cit., p. 266

In conclusion it may be safely affirmed that cellulipetal conduction has been proved for the majority of dendrites, and cellulifugal conduction for the majority of axones, although cellulipetal conduction unquestionably occurs in some parts of some axones. Moreover, it is not unlikely that nerve impulses may pass both ways in axones and dendrites, just as alternating electric currents pass through a copper wire. At any rate, impulses have been shown by physiologic experiments to pass in both directions along a peripheral nerve fibre from the point of stimulation.

(*b*) **Transference of an Impulse from one Neurone to Another.**—A certain amount of stimulation is necessary to call forth a reflex action or to give rise to a sensation. If the stimulus be below this amount, no reflex action or no sensation results. Thus pressure upon a point in the skin may be too slight to elicit the sensation of touch. This is tantamount to affirming that the touch point has a "threshold value." If the neurone theory be in accordance with the facts, then in the spread of an impulse or excitation through the central nervous system one neurone must excite another neurone, and this in turn one or several others. Thus in a certain sense each neurone has a threshold value, called by Goldscheider (1898) the *neurone threshold*. Resistance to the transference of impulses would therefore lie at the points of contact or concrescence of neurones. A point of contact once resistant may doubtless be made less so after many impulses have passed by it. If impulses tend to follow the lines of least resistance, then the neurones concerned would ultimately become intimately associated with each other, and large numbers similarly associated would constitute a beaten pathway for impulses, or, in other words, a tract. The pyramidal cells of the cerebral cortex, for example, doubtless have special connection with some particular cells of the ventral horn of the spinal cord, to which they find it easier to transfer their impulses than to others. Possibly partial recovery after paralysis is due to the passage of impulses along new routes of higher neuronal threshold value than existed in the former pathways. Possibly functional paralysis is sometimes due to an abnormal increase of resistance to transference of impulses at the neuronal threshold.

Fig. 274



Diagrammatic, illustrating the law of multiplication of effect: *a*, dendrite; *b*, axone; *c*, collateral; *e*, cell-body of second neurone. One neurone, *d*, is able to stimulate six secondary neurones.

2. **Law of the Multiplication of Effects.**—It frequently happens that a small stimulus produces a large reaction. For example, a slight tap on the patellar tendon produces a contraction of the entire quadriceps extensor muscle. The explanation is simple, and is illustrated in Fig. 274. Axones give off collaterals, each one of which may be in relation with a separate neurone. In this manner the peripheral sensory neurone in vertebrates is in relation with various levels of gray matter lying between its place of entrance into the spinal cord and its terminal branching at the nucleus gracilis or nucleus cuneatus. By means of these collaterals at least one neurone at each of the various levels may be stimulated. It is likely that

many of these collaterals lie dormant ordinarily, being reserved for emergencies. It is likely, too, that their threshold values are at times too high for transference of impulses, for they may apparently be lowered by drugs, particularly strychnine. A slight stimulus may in strychnine poisoning produce a convulsion, because of the great lowering of resistance at the neuronal threshold. Similarly, the immense multiplication of effect seen in the general convulsion of epilepsy, where a storm beginning gently in a certain motor centre sweeps with tremendously increasing fury over the whole motor cortex of the two hemispheres, and so, involving approximately all of the motor cells of the motor cranial nuclei and of the ventral horns of the cord, may have as its fundamental condition a lowered resistance at the neuronal threshold. Surely Ramón y Cajal's term *avalanche conduction* beautifully describes the law of multiplication of effect.

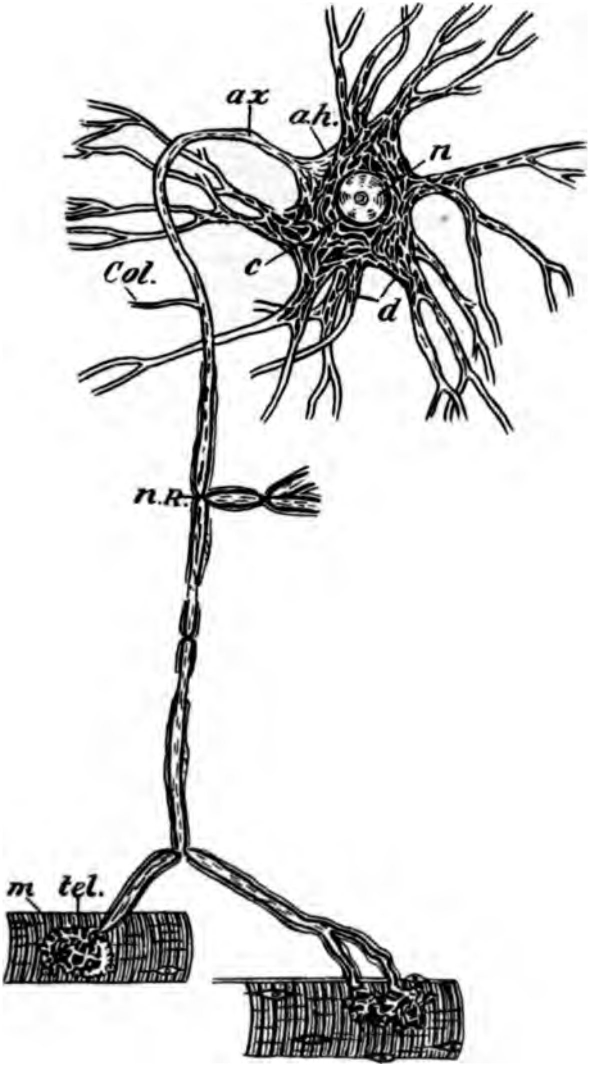
3. **Doctrine of Specific Energy of Nerves; Function of the End Organ; Unity of Nerve Function in Nerves.**—The neuronal protoplasm is probably not equally excited by every irritant. One may regard its qualities of sensitive reaction as so regulated that they respond only to certain forms of irritation, just as certain waves of sound excite vibrations in a cord of a certain length, but not in other cords. This *corresponding susceptibility,* which is entirely hypothetic, may be physically represented by certain states of equilibrium and arrangement of the protoplasmic granules.

The doctrine of specific energies of nerves as formulated by Johannes Müller is based on the fundamental fact that whatever the kind of stimulation employed, whether electric, mechanical, chemical, or traumatic, the character of the response manifested by a given neurone is always constant. For example, no matter what the agent used to stimulate the optic nerve, the response is always a subjective sensation of light and color. Hence, too, if a "cold point" is stimulated, even by a hot wire, a sensation of cold, and of cold alone, results. This constant quality of reaction, despite the variation in the form of external stimulation, has been the cause of much controversy, and has led to two opposing theories.

(*a*) **The End-organ Theory.**—At the distal extremities of peripheral axones and dendrites are specialized structures forming a part of the neurone itself or in close relationship with it. These structures are known as end organs. In the motor neurones they take the form of end plates closely applied to the muscle cells and furnish the medium of communication of the impulse, resulting in the contraction of the muscle fibres. (See Fig. 275.) In the sensory dendrites of the dorsal ganglion cells the end organs assume various forms depending upon the kind of sensation subserved. (See chapter on the Special Senses.)

In this connection the question naturally arises, What determines the quality of the impulses traversing a given neurone? Is it dependent on the cell body, the dendrites, the axone, or the end organs, either separately or collectively? Different forms of stimuli applied to any part of a nerve trunk or its centre produce but one result, and that result depends apparently on the end organ. If it be a motor

Fig. 275



Scheme of lower motor neurone, etc.: *a.h.*, axone hillock devoid of Nissl bodies and showing fibrillation; *ax*, axis cylinder, or axone; *c*, cytoplasm showing Nissl bodies and lighter ground substance; *d*, protoplasmic processes (dendrites) containing Nissl bodies; *n*, nucleus; *n.R.*, node of Ranvier; *Col.*, collateral; *tel.*, motor end plate, or telodendrion; *m*, striped muscle fibre.

nerve, motion in the respective muscle results. If it be a sensory nerve, the sensation customarily excited by that nerve is experienced. Apparently, therefore, the nature of conduction need not vary at all, wherever the neurone may be located or whatever the sensation conducted, but at the terminus of the conducting path the exciting stimulus produces a result dependent upon the character of the end organ or end connections.

Experiments have proved that an isolated nerve conducts equally well in one direction as in the other, and while the mechanical, chemical, and electric stimuli used in the experiments may be neither identical with nor even similar to the natural excitants of nervous impulses, it is perhaps less important to know the nature of the impulse received by a neurone than it is to define its power of transmitting it farther. For example, in a nerve-muscle preparation stimuli of various kinds when applied to the nerve produce contraction in the muscle. Manifestly, here the end plates are of prime importance as constituting the connection between nerve fibre and muscle fibre. And this suggests the idea that, for efferent neurones at least, the end plates alone determine the quality of the nervous impulse. This is comparable with the various recording instruments that may be attached to an electric wire; the agent and the nature of conduction are the same, but the effect varies with the receiver used. In the peripheral sensory neurones the end organs reach a high degree of specialization for the reception of various forms of stimuli. Thus, in the skin the end organs are adapted to the reception of mechanical and thermal stimuli. In the nasal mucosa and the taste buds are found end organs adapted to the reception of chemical stimuli. In the retina are found end organs which are either affected mechanically by the vibrations of the ether, or chemically by the decomposing effect of light.

From these considerations it appears that, while nervous impulses are excited differently according as the sensory end organs (including, of course, those placed deep in the tissues as well as the superficial ones) are adapted to receive impressions, and while, further, the externalization of nervous energy, manifested by motion, secretion, nutrition, etc., depends largely on the peripheral end organs, the character of nervous impulses and the mechanism of conduction never vary and may be identical in all instances.

(*b*) **The Central Theory.**—The opposing school believes that the sort of response evoked in both sensory and motor neurones depends not on the end organ, but upon the central region affected by the stimulus. This is tantamount to affirming that the specific energies belong to the centres and are practically independent of the periphery. Pathologic physiology strongly supports this hypothesis, because irritation of certain cortical areas calls forth certain definite and constant sense perceptions, and in such cases there can be no effect exerted upon the peripheral sensory neurone or its end organ. Odors, flashes of light and color, sounds, even words have been clearly perceived by patients suffering from the pressure of cysts or tumors upon corresponding parts of the cerebral cortex. Evidently the central neurone, in some instances at least, has a specific energy.

Probably, as in all things, truth lies midway. In the gradual development of an individual neurone it undoubtedly establishes its relations with centre and periphery concomitantly. The point is well summarized by Barker:[1] "We cannot think that the various modifications of apparatus mediating between the external physical influence and the most peripheral portions of the sensory neurones of different kinds represent accidental structures which have no physiologic import; nor can we imagine that were the central projection fields in the cerebral cortex, at which the sensory impulses arrive from the different parts of the periphery, of no specific significance for the origin of the different sensations, they would present for the different sensations so absolutely specific a structure."

f. The Inhibitory Power of Neurones.

A familiar example of the inhibitory power of neurones is met with in the motor chain extending from the cerebral cortex to the muscle fibre. The upper motor neurone (archineurone) apparently restrains the lower motor neurone (teleneurone) in its function, as is shown in the phenomenon of the patellar reflex, which is normal only when both neurones are intact. In health this reflex is but moderately active owing to the inhibition said to be exerted by the upper upon the lower motor neurone. If, by disease of the former, the inhibition is lessened or made impossible, then the teleneurone is more free to act, and an increased reflex results. Of course, if the lower motor neurone is destroyed or diseased, the reflex is absent, for there is no path by which the motor impulse can reach the muscle fibre.

It is fair to state that, though physiologists and clinicians in general agree as to the hypothesis of inhibition, very many of them do not agree that the upper motor neurone can inhibit the lower one. Reflexes are increased, for example, in nerve exhaustion. Does such increase mean a decrease of inhibitory power on the part of the upper neurone, or hypersensitiveness of the lower? Surely hyperirritability on the part of the lower neurone, or a diminution of its threshold value are equally competent to lead to increased reflexes. Sectioning of the spinal cord bears on this question. If the upper neurone really inhibits the lower one, when the spinal cord is divided and the fibre of the upper neurone running in the pyramidal tract is therefore severed, thus cutting off the inhibitory impulses from the ventral-horn cells, one would expect increased reflexes. They are, on the contrary, absolutely lost; why, we do not know. Leube believes the patellar reflex is ordinarily a cerebral reflex, instead of a spinal one. When the cerebral path is thus cut off, the spinal reflex is called into play. But the spinal reflex being one never used, though potentially present, becomes a path of relatively increased resistance to conduction. Hence when the patellar tendon is tapped, no knee-jerk results. If the spinal cord is not suddenly severed, as by a stab, but is very gradually divided as by the encroachment of a slowly growing tumor, the reflex is not lost, but is increased from first to last. The explanation by Leube's hypothesis is simple: The pyramidal tract fibres in the cord, being easily compressed and rendered ineffective, the direct spinal reflex is established early; and the spinal reflex being very direct, and requiring few neurones for its accomplishment, the knee-jerk is increased. Thus, according to Leube, there is no necessity for the hypothesis of inhibition. Normally the patellar reflex is a cerebral one, requiring an impulse to make its way up to the cerebral cortex and down again through many neurones, each with its threshold value. Pathologically the short, direct spinal reflex is established, and the neuronal threshold values are so slight that the knee-jerk is relatively increased.

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[1] Loc. cit., p. 255.

g. The Trophic Influence of Neurones upon Tissues.

This influence is one of the most obscure met with in neurology. If the lower motor neurone is divided, or if it undergoes degeneration from poisoning by bacterial toxins, alcohol or metallic poisons (multiple neuritis), rapid wasting of its muscle of supply is the result. The atrophy of the muscle is not the passive wasting of disease; it is an active atrophy, the flesh being lost with great rapidity. On the other hand, division of the upper motor neurone or its impairment by disease does not lead to such atrophy, except in a very few isolated and inexplicable cases. Evidently there can be no question as to the trophic influence exerted by the lower motor neurone upon the muscle fibre which it supplies. The trophic influence, moreover, is not limited to motor neurones. In cases of multiple neuritis with marked sensory disturbances the skin becomes atrophic, of a peculiar appearance, known technically among neurologists as "glossy skin." In diseases of the spinal cord extensive trophic disturbance of the skin and underlying structures may result. For example, in transverse myelitis a bed-sore may rapidly form and attain huge proportions in a few days, or in tabes dorsalis (locomotor ataxia), a trophic ulcer may slowly and painlessly develop under the base of the first phalanx of either great toe.

The trophic influence exerted by neurones upon joints and bones is well known to neurologists. Thus, in cases of tabes dorsalis a knee, an ankle, or an elbow-joint may undergo huge and comparatively painless changes, involving not only the joint, but the bony parts as well. In syringomyelia trophic disturbances, which form one of the cardinal symptoms of its symptomatology, may appear in the large joints as well as in the skin; and not a few cases of ordinary hemiplegia, whether from thrombosis, embolism, or hemorrhage, have been attended with remarkable effusions into the joints, coming on with great rapidity. Most interesting is the *reflex muscular atrophy* seen in joint disease, as, for example, in tuberculosis of the knee. If the knee be diseased, for example, wasting occurs in the quadriceps extensor muscle. That this is an active reflex atrophy and not an atrophy of disuse has been proved by the fact that severing of the sensory fibres from the diseased joint to the spinal cord absolutely prevents such atrophy. According to Charcot, many arthritic diseases are upon a neurologic basis. Indeed, he used to teach that they are first cousins of nervous diseases.

h. Postnatal Neuronic Development.

Constituting what may be designated as a function of neurones, although it is merely a matter of their development, is the supposed ability on the part of certain neurones, notably those of the cerebral cortex, to develop additional dendrites and collaterals and so to form new relationships with cells with which they were not previously connected. On this hypothesis rests the enormous development of the cerebrum of an individual undergoing education, and of this hypothesis further mention will be made under the general subject of aphasia. As such intellectual development depends largely upon the extensive and diverse correlation of existing cells and centres, it will readily be seen how great is the demand for new dendrites and collaterals. Possibly also new axones, if not entire neurones, are required and furnished in a manner as yet unknown. The reverse of the hypothesis is doubtless also true. It is supposed, for example, that dendrites and collaterals may disappear after the particular function subserved by them is no longer required. This is analogous to muscular atrophy from disuse. The wasting of the cortex in general paralysis of the insane favors this hypothesis.

B. THE PHYSIOLOGY OF THE SPINAL CORD.

Physiologically the spinal cord must be considered as extending beyond its gross anatomic limits. Indeed, a better term is cerebrospinal axis, because it indicates that the cerebral stem is merely a continuation of the spinal one. Usage, however, sanctions the term spinal cord, and it will be employed here in its extended sense.

1. THE SPINAL CORD AS A CONDUCTOR OF NERVOUS IMPULSES.

In its function of *conducting nervous impulses* the spinal cord differs from a peripheral nerve in complexity alone. Its fibres, while forming the large tracts comprising the white matter, are precisely similar to those of the peripheral nerves in the function of conduction. We find in the spinal cord, in addition, chains of neurones, the cell bodies of which comprise the gray matter. We have already seen that the cell body of a neurone serves to receive, and possibly to modify, impulses coming to it, and to discharge them through its axone; and while each cell body may be regarded as a centre, it is often merely a midstation, or a relay station, for the reception and transmission of an impulse. All impressions received from the outside world, as well as those coming from the structures of the body itself, and all impulses resulting in motion, secretion, or other manifestation of nervous energy, must pass through the cerebrospinal axis. These may be summed up as *afferent* and *efferent impulses.* The centre toward which the afferent impulses sweep onward in a mighty river called the fillet, into which many tributaries empty, and the centre from which the efferent impulses proceed, is the cerebrum, made up also of neurones. This centre is for the individual the centre of the universe, where are received his impressions of everything external to his body, as well as of the changing conditions of the body itself, and from which emanate all his voluntary and involuntary acts.

a. The Course of Sensory Impulses.

The efferent impulses conducted upward by the spinal cord fall into two great divisions: (I) those of which we are conscious, coming from the peripheral sense organs, general and special; and (II) those of which we are subconscious or not conscious at all, coming from the internal structures of the body. Our visceral impulses are perceived only when they are perverted, in which case we are conscious of discomfort or pain. It is likely that the number of impulses of which we are not conscious vastly outnumber those which we perceive.

(*a*) EXPERIMENTAL PATHOLOGY has been of great assistance in tracing upward through the cerebrospinal axis the paths taken by the sensory impulses. Thus, if one-half of the spinal cord of a monkey is severed, and a few weeks later the animal is killed and the cord stained by Marchi's method, certain fibres will be found degenerated above the section, and certain below. Evidently the former fibres are, according to the Wallerian law, ascending and presumably sensory, while the latter are descending and presumably motor. Not only does experiment upon lower animals thus afford much knowledge of ascending sensory highways, but clinical pathology vastly aids, though lesions in the human cord cannot be produced in definite location at will, and physiologists and anatomists are obliged to wait patiently sometimes for years for opportunities to settle disputed points.

(β) A SECOND METHOD of investigation is that of Flechsig, which is based on the fact that different tracts acquire their medullary sheaths at different periods of embryonic life. As a general law it may be affirmed that those tracts myelinate first which connect the spinal cord with the peripheral sense organs; then, those which connect the various segments of the cord; next, those which connect the cord with the cerebellum; and lastly, those which connect the cord with the cerebral hemispheres. Thus sensory impulses are the first experienced, and motor impulses are the last developed. Applying the general law, proved many times, to embryonic life, sensory strands may be fairly accurately mapped out, and their function determined with reasonable accuracy. By these and other methods it has been demonstrated that in general afferent impulses enter the cord through the dorsal roots and ascend through the dorsal and lateral tracts, while efferent impulses descend through the ventral and lateral tracts and emerge through the ventral roots.

The only sorts of sensory impulses carried upward by the cord are those of common sensation: tactile, algesic, thermal, and muscular. Of the impulses from the organs of special sense only the auditory and gustatory fibres join the cerebrospinal axis; the visual and olfactory impulses have paths of their own to the corresponding cerebral centre for perception of light and odor.

1. **The Course Taken by Impulses of Temperature and Pain,** which are probably intimately associated with each other, is not the same as that taken by the tactile and the muscular impulses. This is proved by the disease known as syringomyelia, in which a centrally developing neoplasm, originating apparently in the substantia gelatinosa centralis, spreads radially so as to involve the gray matter only, ultimately loses its central portion by degeneration and absorption, and so apparently enlarges the embryonic central canal. In this disease a cardinal symptom is the dissociation of tactile sensation on the one hand from thermal and algesic on the other; touch always remains approximately intact, but the ability to distinguish hot from cold and to appreciate pain is lost. The inference is that the fibres carrying impulses of pain and temperature, soon after entering the cord, pass into the gray matter and there arborize about secondary neurones. About the latter much uncertainty prevails.

(*a*) **Through the Gray Matter.**—By some their axones are thought to pass upward through the gray matter itself, and such an inference is not inconsistent with the pathology of syringomyelia and the anatomy of the whole cerebrospinal axis, for such fibres would lie in an area in the cord exactly analogous to the formatio reticularis of the medulla and the tegmentum of the pons, in which ascending sensory fibres are known to be mingled with the gray matter. Indeed, Rossolimo[1] has collected fifteen cases of such dissociation of tactile and thermal sensory impulses in lesions of the medulla and pons involving the aforesaid areas.

(*b*) **The Lateral Limiting Layer.**—By others the axones, after crossing over in the commissure, are thought to extend upward in the lateral limiting layer (lateral marginal zone). The axones are thought to form a series of loops in the lateral column close to the gray matter, and to dip at short intervals into it, there to arborize about the dendrites or cell body of the next higher neurone of the series, its axone forming a second loop, a whole series of neurones arranged in tandem, thus sufficing to conduct the impulses to the fillet.

(*c*) **Through the Anterior Commissure.**—By still others these axones are thought to cross over through the anterior commissure to the opposite side of the cord, there to arborize about cell bodies, the axones of which ascend in the column of Gowers, the so-called anterolateral ascending cerebellar tract. Such is Obersteiner's teaching. All are agreed that the axones carrying impulses of pain and temperature decussate immediately upon entering the cord. The symptomatology of syringomyelia apparently favors the first and second views.

The difficulties in determining the course of algesic and thermal sensations, after they leave the primary neurones, are almost, if not quite, insurmountable; hence the confusion. Even in peripheral nerves a lesion causing more or less motor loss often produces only transitory sensory disturbances. In the higher links of the chain it is possible that lesions may be at once compensated by numerous intercommunications, rendering it difficult by a single lesion entirely to interrupt the sensory path. There may be, for example, the usual highway for the impulses, and one or more potential by-paths, for the opening of which only a slight reduction of the threshold value is necessary. Experiments upon lower animals have not materially advanced our knowledge in this matter, owing to the impossibility of determining accurately the amount or character of the sensory losses experienced by them. It is known absolutely, however, that such impulses cross upon entrance to the contralateral side of the cord, and that they ascend to the fillet. They then follow the mesial fillet to the optic thalamus, where they are received by its ventrolateral nucleus (Monakow's nucleus), the axones from the cells of which further conduct the impulses to the cerebral cortex, to a centre as yet unknown, possibly lying in the superior parietal lobe.

2. **The Course Taken by Tactile Impulses** is similarly obscure. They are known to pass at once, upon entering the cord, to the

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[1] Deutsche Zeitschrift für Nervenheilkunde, March, 1903.

opposite side, but whether through anterior or posterior commissure or both is undecided. Having reached the contralateral side of the cord the tactile impulses doubtless ascend in the lateral limiting layer in large measure, though formerly a few fibres were thought to ascend in the ventral portion of the column of Goll, close to the posterior commissure. Edinger,[1] however, concerning these fibres, asserts that it is positively known that the posterior columns do not conduct tactile impulses. Fig. 277 shows the decussation of the fibres of pain, temperature, and touch.

According to Kölliker some tactile fibres follow a *direct*[2] course, ascending in the lateral limiting layer of the same side. It is extremely likely, however, that such fibres cross to the opposite side at the sensory decussation of the fillet in the medulla. All tactile fibres, therefore, whether decussating immediately upon entering the cord, as the great majority do, or whether decussating at the sensory decussation of the fillet, eventually reach the contralateral mesial fillet. From here the axones proceed to the ventrolateral nucleus of the optic thalamus, ending for the most part by arborization about the cells there located. The dendrites of these cell bodies receive the impulses, conduct them through their corresponding axones upward in the posterior limb of the internal capsule, through the corona radiata to the cerebral cortex, possibly in the motor area, possibly in the parietal region.

3. **The Course Taken by Muscular Impulses.**—These impulses are collected from the muscle mass by peculiar end organs to which the name of neuromuscular bundles has been given, found in all striated muscles, not excepting those of the heart, and found also even in the tendons. From these peripheral sense organs the impulse is carried along the axone-like dendrite of the dorsal spinal ganglion cell to its cell body, thence through its axone into the spinal cord, where, in the column of Burdach, it divides by a Y-shaped division into an ascending and a descending arm. The descending arm quickly makes its way into the gray matter of the segments of the cord immediately below, without constituting any well-defined tract. It was formerly suggested that the comma column of Schultze might represent an aggregated mass of such descending fibres. The evidence is against such a theory, because when the dorsal root is cut between the dorsal ganglion and the cord, no degeneration is found in the column of Schultze. This column can be made to degenerate only upon transverse section of the spinal cord. The ascending limb of the Y-shaped division passes up the column of Burdach, and by the entrance of new fibres at higher levels is gradually forced over into the column of Goll. Thus, such a fibre entering the column of

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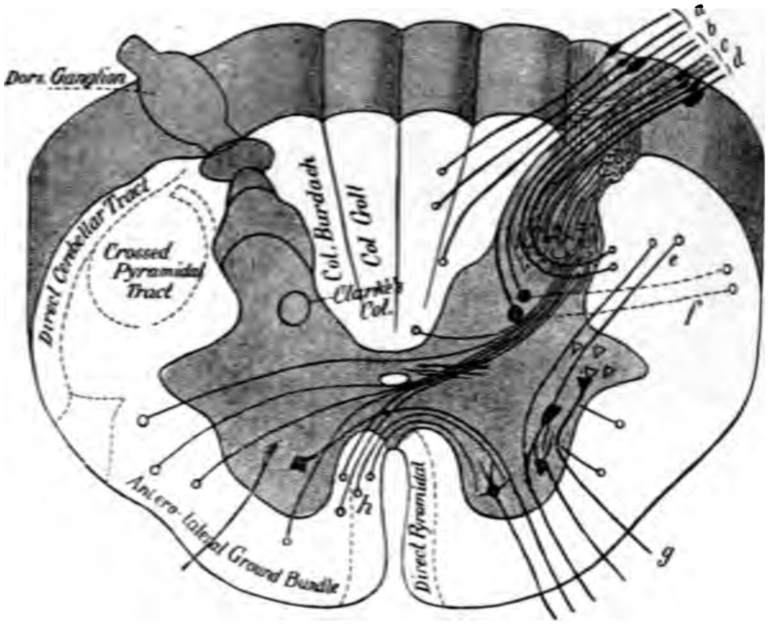
[1] Loc. cit., p. 357.

[2] Fibres which ascend or descend upon the same side of the cord as that which they enter are called direct.

Burdach in the lumbar region will be found in the column of Goll in the cervical cord.

Others of the main fibres entering the cord from the dorsal roots make their way among the cells at the base of the anterior horn, or among the cells of the intermediate gray matter of Gowers, or among the cells of Clarke's vesicular column, about all of which they doubtless arborize. The upper destination of the impulses ascending in the columns of Burdach and of Goll is the cerebral hemisphere of the opposite side. The upper destination of the impulses transmitted to the cells of Clarke's column and to the cells at the base of the posterior horn is the cerebellar hemisphere and worm of the same side. Muscular and somæsthetic impulses, therefore, have open to them two pathways—the cerebral and the cerebellar. (See Fig. 276.)

FIG. 276



Schematic cross-section of the spinal cord, showing destination of the fibres of the posterior roots: *a*, fibres entering the columns of Goll and Burdach, ascending to the nucleus gracilis and nucleus cuneatus *b*, fibres arborizing about the cells of Clarke's vesicular column; *c*, fibres going to Lissauer's marginal bundle; *d*, fibres arborizing about the cells of the posterior horn; *e*, fibres from the crossed pyramidal tract arborizing about the cells of the ventral horn; *f*, fibres proceeding from Clarke's nucleus to the direct cerebellar tract; *g*, axones from the motor cells of the ventral horn leading to the muscles; *h*, fibres from the direct pyramidal tract crossing in the anterior commissure to the opposite ventral horn. (After Edinger.)

(*a*) **The Cerebral Pathway.**—The muscular and somæsthetic impulses pass up the axones of the dorsal spinal ganglion cells through the column of Burdach and of Goll. These axones for the most part arborize about the cells of the nucleus gracilis and nucleus cuneatus of the same side, and to these cells the impulses are without doubt transmitted. (See Fig. 277.) The axones from the cell bodies of the nuclei, known as the internal arcuate fibres, decussate *en masse* in the medulla, forming the sensory decussation or the decussation of the fillet. Thus the impulses are transmitted to the opposite side of the body, and they then proceed upward through the fibres of the mesial fillet to the cell bodies of the ventrolateral nucleus of the optic thalamus, from which they are retelegraphed upward through the internal capsule and corona radiata, to the motor area of the cerebral cortex, chiefly to the small pyramidal cells according to Victor Horsley. It will be observed that each fibre destined for the cerebrum crosses from one side of the cerebrospinal axis to the other. This is in accordance with the general law of decussation of cerebrospinal fibres, whether ascending or descending.

FIG. 277

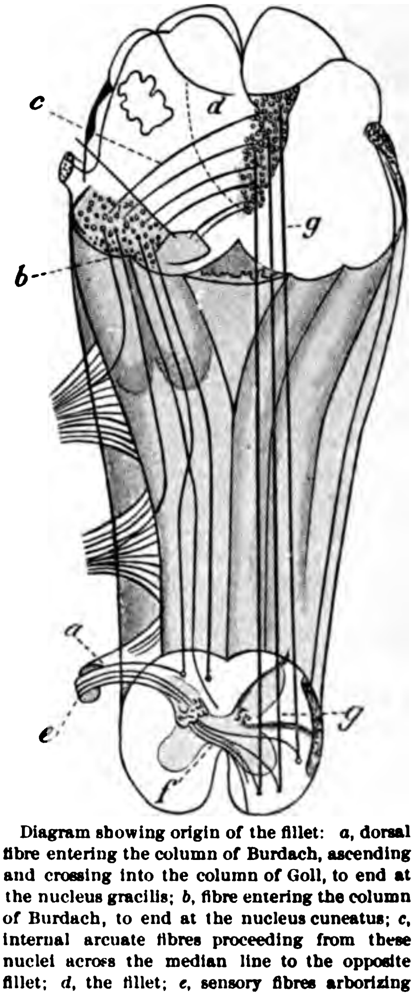


Diagram showing origin of the fillet: *a*, dorsal fibre entering the column of Burdach, ascending and crossing into the column of Goll, to end at the nucleus gracilis; *b*, fibre entering the column of Burdach, to end at the nucleus cuneatus; *c*, internal arcuate fibres proceeding from these nuclei across the median line to the opposite fillet; *d*, the fillet; *e*, sensory fibres arborizing about the cells of the posterior horn; *f*, axones proceeding from these cells to the opposite lateral limiting layer, thence passing (*g*) to the fillet. Thus all fibres entering the dorsal root reach the fillet of the opposite side. (Edinger.)

(*b*) **The Cerebellar Pathway.**—The cerebellum is an organ which, among other things, harmonizes and co-ordinates muscular movements. It is, therefore, highly fitting for fibres conveying muscular impulses to make their way into the cerebellum. For these fibres no law of decussation holds. The impulses from one side of the body proceed upward through the corresponding side of the cord to the same side of the cerebellum, and the tracts conveying them are called *direct* on that account. There are evidently three definite pathways from muscles to cerebellum:

(I) Certain of the ascending Y-shaped fibres which pass up the columns of Burdach and Goll apparently do not arborize about the cells of the nucleus gracilis or nucleus cuneatus, but instead emerge from the dorsal part of the medulla and proceed into the corpus restiforme of the same side, and thence into the cerebellum under the name of the dorsal external arciform fibres (fibræ arcuatæ dorsales externæ).

(II) Doubtless the largest mass of spinocerebellar fibres conveying muscular impulses passes up the direct cerebellar tract. The impulses enter through the dorsal root and are conveyed to the cells of Clarke's vesicular column, the axones of which proceed outward through the gray matter of the cord, to form the direct cerebellar tract, by means of which, therefore, the impulses are enabled to reach the vermis cerebelli, especially its dorsal and proximoventral portion.

(III) A small number of fibres, according to some observers, transmit muscular impulses upward to the cerebellum by way of the so-called anterolateral ascending cerebellar tract which lies in the area occupied by the *mélange* of fibres known as Gowers' tract. This particular cerebellar tract apparently passes upward to the anterior extremity of the pons, and then proceeds backward through the superior cerebellar peduncle beside the valve of Vieussens, to end in the ventral and distal dorsal part of the worm and the lateral lobe of the cerebellum. It has been proposed to call the direct cerebellar tract the dorsolateral direct cerebellar tract, and that tract which runs in Gowers' tract the ventrolateral direct cerebellar tract.

b. The Course of Motor Impulses.

The cord is a conductor of motor impulses from two sources, the cerebrum and the cerebellum. Impulses from the cerebrum are those concerned with voluntary motion; impulses from the cerebellum are those concerned with the co-ordination of various muscles in the execution of a voluntary act. Each set of impulses has a pathway of its own.

1. **The Course Taken by Voluntary Impulses from the Cerebral Cortex.**—These originate in the large pyramidal cells of the motor cortex and descend along their axones, from the pyramidal tracts, through the knee and anterior two-thirds of the posterior limb of the internal capsule, through the medial third of the pes pedunculi to the ventral part of the closed medulla, where the majority of the fibres decussate, forming the decussation of the pyramids and giving rise to the crossed pyramidal tract which descends to the lowermost portion of the spinal cord. Such fibres as do not decussate proceed downward on the same side of the cord under the name of the direct pyramidal tract. These two sets of axones convey motor impulses originating in the cells of the cerebral motor cortex to the motor cells

of the anterior horn, about which they arborize; and these cells retelegraph the message through their peripheral axones to the particular muscle fibres to be stimulated. The motor end plate, familiar to the student from histologic study, is the device by which nerve energy is converted into muscular action, and is functionally precisely what a motor is to an electric current—a transformer of one sort of energy into another. (See Fig. 278.)

It is but just to state that von Monakow is of the opinion that the pyramidal tract cells do not directly transmit their impulses to the motor cells of the ventral horn. He believes that an associational neurone, lying within the gray matter of the cord, is intercalated between the terminal arborization of the axone of the pyramidal cell and the motor cell of the ventral horn, basing his belief upon the absence of degeneration in the gray matter when the pyramidal fibres are severed. Most investigators deny this contention, and conceive of the motor chain as a two-link affair, consisting of an upper and of a lower motor neurone. It is usually asserted, too, that the fibres of the direct pyramidal tract invariably decussate through the ventral or white commissure, so that ultimately each and every fibre crosses to the opposite side of the cord. This is undoubtedly not in accordance with the fact, for it is positively known, both from experimental and clinical evidence, that numerous uncrossed fibres descend even in the so-called crossed pyramidal tracts.

2. **The Course Taken by the Co-ordinating Impulses from the Cerebellum.**—Concerning the course of these fibres much confusion reigns, owing to the varying results obtained by different investigators. There are two distinct views as to the pathway followed by impulses from the cerebellum to the cord.

(I) The older view is that cerebellar impulses make their way through what used to be called the anterolateral descending cerebellar tract or tract of Löwenthal, first mentioned by him in 1886, though first thoroughly studied by Marchi in 1891. Marchi believed that these fibres came mainly from the vermis, that they passed through the middle cerebellar peduncle into the pons, and then by way of the posterior longitudinal bundle and the interolivary layer of fibres into the ventrolateral column of the cord. Marchi's conclusions were based upon descending degenerations in the cord after removal of the cerebellar hemisphere. Ferrier and Turner declared that such degeneration took place only when the nucleus of Deiters was injured; that if the cerebellar hemisphere be removed without injury to the nucleus of Deiters no such degeneration follows. On the other hand, Biedl favors Marchi's opinion and states that he can follow such a tract almost as far as the sacral end of the cord.

(II) The second view, until recently somewhat in the ascendancy, regards the vestibulospinal path as the one down which impulses pass from cerebellum to cord. The axones from this tract issue

FIG. 278

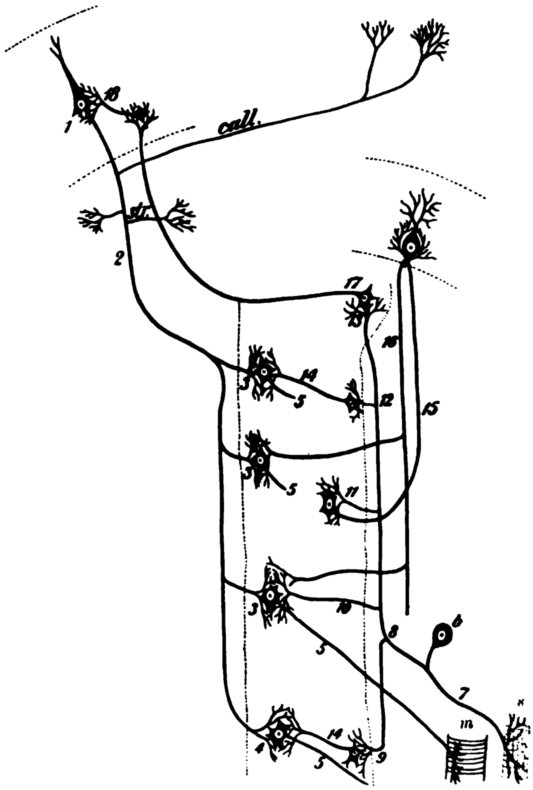


Diagram showing the probable relations of some of the principal cells of the cerebrospinal system to one another: 1, a cell of the cortex cerebri; 2, its axis cylinder or nerve process passing down in the pyramidal tract and giving off collaterals, some of which, 3, 3, end in arborizations around cells of the anterior horn of the spinal cord, the main fibre having a similar ending at 4; *call.*, a collateral passing to the corpus callosum; *str.*, another passing to the corpus striatum; 5, axis-cylinder process of anterior cornu cell passing to form a terminal arborization in the end plate of a muscle fibre, *m;* 6, a cell of one of the spinal ganglia. Its axis-cylinder process bifurcates, and one branch, 7, passes to the periphery to end in an arborization in the sensory surface, *s*. The other (central) branch bifurcates after entering the cord (at 8), and its divisions pass upward and downward (the latter for a short distance only); 9, ending of the descending branch in a terminal arborization around a cell of the posterior horn, the axis-cylinder process of which, again, ends in a similar arborization around a cell of the anterior horn, 10, a collateral passing from the ascending division directly to envelop a cell of the anterior horn; 11, one passing to envelop a cell of Clarke's column; 12, a collateral having connections like those of 9; 13, ending of the ascending division of the posterior root-fibre around one of the cells of the posterior columns of the bulb or medulla oblongata; 14, 14, axis-cylinder processes of cells of the posterior horn passing to form an arborization around the motor cells; 15, a fibre of the ascending cerebellar tract passing up to form an arborization around a cell of the cerebellum; 16, axis-cylinder process of this cell passing down the bulb and cord, and giving off collaterals to envelop the cells of the anterior horn; 17, axis-cylinder process of one of the cells of the posterior column of the bulb passing as a fibre of the fillet to the cerebrum, and forming a terminal arborization around one of the smaller cerebral cells; 18, axis cylinder process of this cell, forming an arborization around the pyramid cell, 1. (Schäfer.)

from the cells of the nucleus vestibuli lateralis or Deiters' nucleus, and possibly from Bechterew's nucleus also. They then proceed down the cord, where they may be traced in the ventrolateral column, just ventral to the ventral horn. They have been traced into the gray matter, where they have been seen to arborize about the cells of the anterior horn.

(III) Both views are beautifully harmonized by Thomas, of Paris, who agrees with Biedl in some respects, and differs in others. He places the origin of the cerebellospinal fibres in the cells of the corpus dentatum cerebelli, and says that their axones pass down through both Bechterew's and Deiters' nuclei, and thence by way of the formatio reticularis to the ventrolateral column of the cord, to end by arborizing about the cells of the ventral horn, to which they deliver their impulses of co-ordination. Thomas has further found that if, along with the corpus dentatum, the nuclei of Bechterew and of Deiters are injured, the descending degeneration is more extensive. Thus both views are reconciled. The judgment of the writer is that this pathway is essentially the one taken by the cerebellospinal impulses.

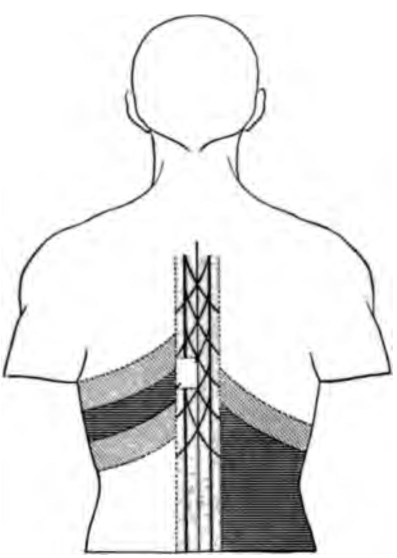
c. Pathologic Physiology of the Cord.

To Gowers we owe the exceedingly great service of clearly formulating the effects of lesions upon the upper and lower motor neurones. Disease or destruction of the lower motor neurone causes flaccid paralysis, absence of the tendinous reflexes, atrophy of the paralyzed muscles, and electric reactions of degeneration. Disease or destruction of the upper motor neurone produces spastic paralysis, exaggeration of the tendinous reflexes, no atrophy of the paralyzed muscles, and no electric reactions of degeneration.

To Brown-Séquard is due the enunciation of the clear-cut symptomatology produced by a transverse lesion through one-half of the spinal cord. Since the crossed pyramidal tract is cut there is complete paralysis on the same side below the lesion. Since the direct pyramidal tract is cut there is usually a slight paralysis on the opposite side below the lesion, because fibres which are about to cross to the opposite side through the white commissure are cut off. Since a few motor cells of the anterior horn are cut, theoretically there should be atrophy of the particular muscle fibres supplied by them; but clinically such atrophy can seldom be detected because of its limited extent.

The sensory losses are very interesting. Since the lateral limiting layer and Gowers' tract are both severed, impulses of touch, temperature, and pain, which have entered the cord on the opposite side, are entirely cut off; therefore, there is tactile anæsthesia, thermæsthesia, and analgesia on the whole surface of the body below and on the side opposite the lesion. Moreover, the sensory roots which enter the cord at the site of the lesion are destroyed; hence, there is upon the same side of the body a narrow band of tactile anæsthesia, thermæsthesia, and analgesia at the exact level of the lesion. Furthermore, the sensory roots which enter the cord just above and just below the lesion are thereby put into a state of hyperirritability, so that both above and below this narrow band are similar narrow bands of hyperæsthesia, hyperthermæsthesia, and hyperalgesia. A similar hypersensitive band is for the same reason found above the level of total anæsthesia on the side of the body opposite the lesion. A study of Fig. 279 will make these points clear. A further sensory symptom remains. Impulses of muscular sense were described as ascending on the same side of the cord as that which they enter. Since these impulses will be cut off by hemisection of the cord, there will be complete absence of the muscular and somæsthetic sense on the same side as the lesion and below it. In brief, therefore, there are the following symptoms: (*a*) paralysis of all muscles on the same side, below the lesion; (*b*) loss of the muscular and somæsthetic sense on the same side, below the lesion; (*c*) loss of the tactile, thermic, and algesic senses on the opposite side, below the lesion; (*d*) a narrow band of anæsthesia, thermæsthesia, and analgesia on the same side, at the exact level of the lesion; (*e*) narrow bands of increased irritability, both above and below (*d*); (*f*) a narrow band of increased irritability above the level of complete anæsthesia, on the side opposite the lesion.

FIG. 279



Anæsthesia is indicated by horizontal lines; hyperæsthesia by diagonal lines. (Brissaud.)

2. THE SPINAL CORD AS A REFLEX CENTRE.

By virtue of its conductive function, which is differentiated in degree only from that of peripheral nerves, the spinal cord possesses another function distinctive in itself. A sensory impulse entering the cord by the axone of a dorsal spinal ganglion cell, instead of ascending to the cerebral cortex and becoming an element of consciousness, may be conducted directly or by collaterals to the motor cells of the anterior horn. This is a short circuit and forms the path taken by those subconscious sensations which arouse involuntary muscular contraction, giving us the phenomenon called *reflex action*. In some conditions of disease and in certain forms of intoxication every voluntary muscle of the body may be made to contract reflexly, while in other diseased conditions and intoxications reflex action may be diminished or entirely lost.

a. Reflex Action.

1. **General Considerations.**—The mere presence of reflex action is indicative of the fact that the motor and sensory terminal neurones with their collateral branches of communication are intact. Loss of reflexes implies an interruption to this circuit, called the reflex arc. And as the arc is composed of a sensory neurone and a motor neurone, with or without the intercalation of an associational neurone, the lesion may be located in any one of the two or three neurones, or in any of their conducting parts, axones, collaterals, or dendrites. If there be a lesion of the motor arm of the reflex arc, not only is reflex action lost, but also voluntary action, and complete motor paralysis is present in the part. If reflex action alone is lost, while voluntary action is possible, the lesion must be in the sensory arm of the reflex arc. In the latter case other sensory disturbances are to be looked for.

Reflex action constitutes in its varied forms a most important part of the life of every animal. In the lowest organisms it is of paramount value, the relations existing between stimuli received from the environment and the reactions thereto on the part of the animal making up the sum of its existence. Ascending the scale of development, reflex actions multiply in number and diversity, and there is gradually evolved an additional higher form of nerve centre than that concerned in reflex action, one which provides for the storing up of impressions, for comparisons between them, and for all the phenomena of psychic activity. Instinct must be looked upon as more or less complicated reflex action, and is merely the physiologic expression of inherited mutual relationships between certain sensory and certain motor groups of neurones. Instinctive movements are invariably reflex ones, and hence are executed before the necessity for them is appreciated by the higher cerebral centres.

In the presence of these more highly developed cerebral centres, the subsidiary centres of reflex action have not become less important for the life of the individual, even if somewhat overshadowed. In human physiology we find reflex action forming the basis of the vegetative functions, so-called, and so well developed, indeed, that in the absence or loss of the higher psychic centres, life is still continued by reason of the activity of the reflex centres in the medulla spinalis and oblongata. Under the chapters on Respiration and

Circulation (*q. v.*) it will be found that these vital functions depend on the condition of aeration of the blood. That provides the stimulus to the respiratory and circulatory centres in the medulla; and by reflex action, resulting in the necessary contraction and relaxation of the muscles of the chest walls and the heart, these phenomena recur in a continuous succession of cycles, so that life is prolonged.

2. **Purposeful Character of Reflex Action.**—In observing results of experiments on animals the purposeful character of the reflexes is striking. This purposeful character is not due to mental deliberation and consequent well-directed action, but is due to the inheritance of definite anatomic pathways from sensory to motor neurones. An excellent example of such purposeful movements, in which possibility of cerebral action is excluded, is seen in the protective movements of pithed or decapitated frogs. If a drop of dilute acid be applied to the skin of such a frog, it strives to get rid of the offending body and it generally succeeds. Thus when a drop of acid is placed on the right flank of a brainless frog, the right foot is almost invariably used to rub off the acid. If the right foot be cut off or otherwise hindered from rubbing off the acid the left foot is, under exceptional circumstances, used for this purpose. This at first sight appears like an intelligent choice; indeed, so purposeful are these acts and the actions of groups of muscles so adjusted to perform a particular act that Pflüger long ago regarded them as directed by and due to consciousness of the spinal cord. If many instances occurred where evidences of a variable automatism which we call volition were manifested by the cord, we should be led to believe that the choice was determined by an intelligence. But, as has been abundantly observed, a frog in which the brain has been removed, having only the spinal cord, makes no spontaneous movement.

Similar reflex movements are observed in mammals, though not to such an extent as in frogs. In dogs in which partial removal of the cerebral hemispheres has apparently heightened the reflex excitability of the spinal cord, the remarkable scratching movements of the hind leg which are called forth by stimulating a particular spot on the loins or the side of the body are exerted by the leg of the opposite side if the leg of the same side be gently held. In this case the vicarious movements are ineffectual, the leg not being, as in the case of the frog, crossed over so as to bear on the spot stimulated, and this, therefore, cannot be considered as an act of wholly purposeful character.

3. **The Mechanical Character of Reflex Action.**—The majority of simple reflexes are mechanical rather than facultative, even though they seem to be the latter. For example, if a flame be applied to the side or part of the body of an eel, the body is moved away from the flame. Such a reflex movement is apparently purposeful. If the body of a decapitated snake is brought into contact at several places

with an arm or stick, complex reflex movements are excited, the effect of which is to twine the body around the object; and this reflex seems purposeful rather than mechanical. Yet a decapitated snake will, with fatal readiness, twine itself around a red-hot iron.

4. **Summation of Stimuli.**—In all reflex movements, whether of a simple or complex nature, the response is in proportion to the strength and nature of the stimulus; that is, the afferent impulse. A single weak stimulus, moreover, which in itself is incapable of discharging a reflex act, may if repeated sufficiently often bring about such a discharge. The single stimuli are apparently added together until an amount is reached sufficient to excite the reflex act. The process of summation doubtless takes place in the cord. This law possibly is exemplified in Jacksonian epilepsy, where a particular area of the motor cortex under irritation, gradually sums up its irritating stimuli until the motor discharge or convulsion takes place. It is believed by some to be extremely probable that all reflex acts are due to the reception and addition of repeated impulses on the part of the nerve centres.

5. **The Time Required for Reflex Actions.**—In the frog, deducting the time taken in the transmission of impulses along nerves, the time consumed in the cord (reflex time) varies from 0.008 to 0.015 second; if the reflex crosses to the other side it is one-third longer. It is lessened by heat, and by the influence of a strong stimulus. The rate of transmission in the peripheral nerves is approximately 90 feet per second.

6. **Inhibition of Reflexes.**—Within the body there are mechanisms which can suppress or inhibit the discharge of reflexes, and they may therefore be termed mechanisms of inhibition.

(*a*) **Voluntary Inhibition.**—The observations of every-day life teach that reflex acts can be inhibited to a certain extent by action of the will. The eyelids may be kept open when the eyeball is touched; movement of a part may be arrested when the skin is tickled. If, however, the stimulus be strong and is repeated with sufficient frequency, the reflex impulse ultimately overcomes the voluntary effort. Inhibitory acts are not all similar in character; for example, when we voluntarily stop the muscular acts which result from tickling the sole of the foot, we achieve this by throwing into action an opposing group of muscles, but it is doubtful whether inhibition is to be wholly explained as a matter of muscular antagonism. When the brain of a frog is removed and the effects of a shock have passed off the reflex excitability of the animal is found to be increased. This suggests the idea that in the intact nervous system the brain is exerting some inhibitory influence on reflex actions. If a frog from which the cerebral hemispheres have been removed (the optic lobes, bulb, and spinal cord being left intact) be tested by applying a drop of acid on its skin, it will be found that the reflex excitability is increased. If, however, the optic lobes be stimulated by applying a crystal of salt the reflex acts are prolonged or suppressed. Similar results may be obtained by stimulating in mammals the corpora quadrigemina, which bodies are analogous to the optic lobes of frogs.

(*b*) **Beyond Voluntary Inhibition** are those reflex movements which cannot at any time be performed voluntarily. Thus erection, ejaculation, parturition, and the movements of the iris are neither direct voluntary acts, nor can they, when they are excited reflexly, be suppressed at will. It is true, however, that some nervous centres such as the respiratory may be, to a certain extent, under the control of the will. Thus we can hold our breath or completely inhibit respiration for a time, or we can increase our respiratory rate at will; yet we do not have the absolute power of voluntary inhibition. No one can commit suicide by voluntarily inhibiting respiration. In the same manner the micturition centre may for a long time be successfully inhibited, but not indefinitely. A time comes when the centre is beyond voluntary inhibition.

(*c*) **Unconscious Cerebral Inhibition** is a prominent feature of reflex action. Strong stimulation of a sensory nerve inhibits reflex movements. If the toes of one foot of a frog are dipped into dilute sulphuric acid at a time when the sciatic of the other leg is being powerfully stimulated with an interrupted current, the period of incubation of the reflex act will be found to be much prolonged and in some cases the reflex withdrawal of the foot will not take place at all; and this holds good not only in the complete absence of the optic lobes and bulb, but also when a portion of the spinal cord, sufficient to carry out the reflex action in the usual way, is left intact. Evidently the brain is constantly exerting an inhibitory action over spinal reflexes, and, being in this experiment wholly absorbed in the perception of painful sensory impulses from one territory, neglects to lift the barrier of inhibition as it customarily does.

7. **Types of Reflexes.**—Reflex movements may be divided into the three following groups: (*a*) simple or partial reflexes; (*b*) extensive inco-ordinated reflexes or reflex spasms; (*c*) extensive co-ordinated reflexes.

(*a*) **The Simple or Partial Reflexes** are characterized by the fact that stimulation of a sensory area discharges movements in one muscle only, or at least in one limited group of muscles—*e. g.*, contact with the conjunctiva causes closure of the eyelids.

(*b*) **The Extensive Inco-ordinated Reflexes or Reflex Spasms.**—These movements occur in the form of clonic or tetanic contraction in individual muscles, or all of the muscles of the body may be implicated.

CAUSES.—A reflex spasm depends upon a double cause: (1) The gray matter of the spinal cord may be in a condition of exalted excitability so that the nervous impulse, after having reached the centre, is easily transferred to the neighboring centres. This excessive excitability is produced by certain poisons, more especially by strychnine, brucine, caffeine, atropine, nicotine, carbolic acid, tetanin. The slightest touch applied to an animal poisoned with strychnine is sufficient to throw the animal at once into spasms. Pathologic conditions may cause similar results, as in hydrophobia and tetanus.

(2) Extensive reflex movements may also take place when the discharging stimulus is very strong. For example, this condition occurs in man when in great pain; thus, intensive neuralgia may be accompanied by extensive spasmodic movement—tic douloureux.

(*c*) **Extensive Co-ordinated Reflexes** are due to stimulation of a sensory nerve causing the discharge of complicated reflex movements, in whole groups of different muscles, the movements being orderly, co-ordinated, and far-reaching. An excellent example of such a reflex is seen in the purposeful reflex of a decapitated frog already mentioned. If such movements were not co-ordinated they would be irregular and ineffectual. There is reason to believe that this co-ordination in the movements of voluntary muscles takes place in the part of the spinal cord which carries out the movement, and not in the cerebral hemispheres, though under normal conditions the latter may be conscious of the whole movement, including its co-ordination. Such extensive co-ordinated reflexes may occur in man during sleep, or they may occur pathologically as in epilepsy and hysteria. Such reflexes are more easily and completely discharged when the end organ of the sensory nerve is stimulated than when the nerve trunk itself is irritated; for example, gently tickling the skin of the sole of the foot brings out a greater amount of reflex activity than stimulation of the trunk of the internal plantar nerve.

b. The Reflexes.

The reflexes are customarily divided into the superficial or cutaneous, the deep or tendinous, and the organic or visceral reflexes.

1. **Superficial Reflexes.**—(*α*) PLANTAR; elicited by stroking or scratching the sole of the foot, which causes attempts to withdraw the foot from the source of irritation.

(*β*) GLUTEAL; a contraction of the gluteal muscles *en masse* when the buttock is gently pricked or scratched.

(*γ*) CREMASTERIC; when the thigh is irritated on its inner surface by grasping, stroking, scratching, etc., the homolateral testicle is distinctly elevated.

(*δ*) ERECTILE REFLEX OF PENIS; produced by gentle friction of the glans penis, especially of the frænum, resulting in turgidity of the organ and erection. Its analogue in the female pertains to the erection of the clitoris.

(ε) Abdominal; consisting of a retraction of the anterior abdominal walls when the skin is slightly irritated.

(ς) Laryngeal; irritation of the lining of the larynx, trachea, or bronchi produces coughing.

(η) Pharyngeal; attempts to extrude contents of the pharynx, even to the point of vomiting, when the fauces or lining of the pharynx is stimulated.

(θ) Nasal; causing sneezing when the nasal mucous membrane is irritated.

(ι) Conjunctival; closure of the eyelid when anything foreign touches the conjunctiva or the eyelashes.

Pathologic Cutaneous Reflex.—Babinski's toe phenomenon is obtained by gently stroking the outer portion of the sole with the point of a lead-pencil or stylus; the reflex is manifested by the extension of the great toe. When present it is a sign of exceedingly great value to the clinician, for its presence signifies disease of the pyramidal tracts, or of the upper motor neurone.

2. **Deep Reflexes.**—(α) Tendo Achillis Reflex.—If the patient kneels upon a chair, facing its back, allowing his feet to hang over the edge of the seat, a tap upon the tendo Achillis will cause contraction of the soleus muscle,[1] and the heel will be jerked up. Tested in this manner the reflex is invariably present in health. In diseases causing disappearance of the patellar reflex, the tendo Achillis also disappears.

(β) Patellar Reflex (Knee-jerk).—When the thigh is supported by the hand or is crossed over the other thigh, and the leg is flexed at the knee, thus securing relaxation of the quadriceps extensor, a tap on the tendon just below the patella causes the leg to be suddenly extended. This reflex is normally present, but its exaggeration and its loss are both indicative of disease.

(γ) Triceps Reflex (Elbow-jerk).—This is analogous to the knee-jerk and is elicited by supporting the arm over the back of a chair, the forearm being flexed, and then by tapping the triceps tendon just above the olecranon. In health it is usually present. Its exaggeration or its absence may be indicative of disease.

(δ) Biceps Reflex.—If the flexed forearm be supported at the elbow, the wrist slightly flexed and also supported, tapping on the tendon of the biceps sometimes causes contraction of the muscle.

(ε) Scapulohumeral Reflex.—If the scapula be sharply tapped at the junction of the spine and the vertebral border, or at its inferior angle, an extensive movement of shoulder and arm with slight external rotation of the latter sometimes takes place.

(ς) Inferior Maxillary Reflex.—If the mouth be partly opened and a flat instrument or a lead-pencil resting upon the lower teeth be tapped, occasionally the lower jaw is slightly and sharply raised by a reflex movement.

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[1] According to S. Weir Mitchell, the gastrocnemius takes no part in this reflex.

Pathologic Reflexes. (*α*) ANKLE CLONUS.—If the half-extended leg be somewhat supported at the knee, and the ball of the foot be suddenly pressed up, putting the tendo Achillis on a stretch, in certain instances there results a series of clonic contractions of the calf muscles with consequent alternate extension and flexion of the foot, which continues as long as pressure is maintained on the ball of the foot and ceases as soon as the foot is released from pressure. It is never present in health, and indicates involvement of the pyramidal tracts. It is a very reliable clinical sign when present, but does not occur nearly so frequently as the Babinski toe phenomenon of similar import.

(*β*) PATELLAR CLONUS.—In conditions of exaggerated knee-jerk, if the forefinger be applied above the patella and the latter pressed down with a sudden movement, sometimes a clonic contraction of the quadriceps occurs and the patella is alternately raised and lowered.

3. **Organic Reflexes.**—Under this head are included many of the functions of different organs of the body, on which the well-being of the organism as a whole depends, some of them indeed being of vital importance. Like the superficial and deep reflexes they are expressed by muscular activity, but unlike them usually the synergic function of several groups of muscles is required for their execution.

(*a*) **Reflexes of the Alimentary Tract.** (*α*) SUCKING.—When the mother's nipple is placed in the mouth of a newborn infant and a few drops of colostrum tasted by it, there ensues a form of peristaltic, vacuum-producing movement of the tongue and lips, which is reflex in nature.

(*β*) DEGLUTITION.—The presence of food in the back part of the mouth and in the pharynx brings on successive dilatations and contractions in the segments of the œsophagus from above downward, constituting the act of swallowing. Only the initial part of this act is under voluntary control. The rest is purely reflex.

(*γ*) GASTRIC MOVEMENTS.—These are induced by the presence of food in the stomach, and, as is well known, serve as an important factor in gastric digestion. Closely associated with them and yet distinct from them is the:

(*δ*) PYLORIC REFLEX, by virtue of which the contents of the stomach are retained until gastric digestion is complete. It consists of a firm contraction of annular muscle fibres, and of a subsequent relaxation of these fibres, permitting the stomach contents to pass into the duodenum.

(*ε*) INTESTINAL MOVEMENTS.—These are perhaps not to be dis-associated from those of the stomach, which they resemble. They, too, are similarly caused by the presence in them of ingested food.

Whether a separate reflex act, or accomplished by the aid of duodenal peristalsis, the emptying of bile from the gall-bladder into the bowel is probably reflex. The presence of muscle fibres in its walls would point to this.

(ς) DEFECATION.—While to a certain extent a voluntary act, defecation is reflex to a degree. Indeed, it is highly probable that the inhibition of the act of emptying the rectum is the voluntary act, while the withdrawal of the inhibition (relaxing the sphincter ani) permits the act of defecation to be accomplished either entirely reflexly or by the aid of the voluntary action of the diaphragm and abdominal muscles.

It will be seen that these reflexes connected with the alimentary canal may all be included under two forms of muscular activity: peristalsis and constriction. Strictly speaking, annular contraction of the alimentary tube—constriction—is a part of peristalsis, but, as exemplified by the cardiac and pyloric ends of the stomach and by the sphincter ani muscles, constriction must be distinguished as a separate reflex act.

Pathologic Reflexes. (*α*) EMESIS.—This is a reflex very complicated in mechanism. In its simplest form it arises from irritant ingesta exciting spasmodic contraction of the stomach and extrusion of its contents through the relaxed œsophagus. But many other stimuli are capable of producing the motor phenomenon of vomiting. Thus nauseating odors, certain visual impressions, such as the sight of blood, or of objects which are associated in the memory with a former nausea, are examples of the numerous sensory avenues through which the emetic reflex may be excited.

(*β*) DUODENAL REGURGITATION.—This may accompany the preceding or it may occur independently of it. Usually, however, it results in vomiting, as the presence of bile in the stomach is irritating, producing nausea.

(*b*) **The Genitourinary Tract.** (*α*) MICTURITION.—This act is allied to that of defecation, being voluntarily inhibited, and taking place reflexly on the withdrawal of the inhibition (relaxation of the vesical sphincter).

(*β*) SEMINAL EMISSION.—In the male this may be a purely reflex act or it may be led up to by voluntary movements. In the latter case, illustrated by coitus, when the excitation of the glans penis has reached a certain stage the reflex contractions of the ejaculatory muscles proceed without possibility of further voluntary inhibition. In sleep the act may occur as a purely reflex one, the stimulus being supplied by too great warmth of the parts, irritation within the vesicourethral canal, or subconsciously by dreams.

(*c*) PARTURITION.—The gravid uterus is capable of voiding its contents independently of voluntary control, as demonstrated in cases of transverse lesion of the cord above the parturition centre.

Usually in the second stage of labor, voluntary muscular contraction in the diaphragm and abdominal walls reinforces the reflex act.

(*c*) **The Pupillary Reflex.** (*α*) Light Reflex.—When the light entering the eyeball is suddenly increased in intensity, the iris contracts, leaving a smaller pupil. Conversely, a sudden diminution of light intensity leads to an enlargement of the pupil.

(*β*) Accommodation Reflex.—When an object seen at a distance of two feet or more is quickly moved up near the eyes, and the gaze be fixed on it, the eyes converge and the pupils become narrow. Conversely, when an object near the eyes is suddenly removed for some distance, the eyes diverge and the pupils dilate. Thus sight is accommodated to distance.

(*γ*) Sympathetic Pain Reflex.—When the skin of the side of the neck is painfully irritated, the pupil expands in some individuals.

Pathologic Reflex (Argyll-Robertson Reflex).—In this condition the pupil reacts perfectly to accommodation, but is absolutely inactive under the influence of light. Such a reflex is a cardinal symptom of locomotor ataxia, although it also occurs in cerebral syphilis, general paralysis of the insane, and even in intense alcoholism.

(*d*) **The Circulatory System.**—Throughout the system of bloodvessels of the body we find an accompanying intricate nerve supply, through which medium the muscular walls of the bloodvessels are influenced to contract or to relax, and so control the volume of blood in a given part. In the heart there are met everywhere in its muscular walls nerve fibres originating in the cardiac ganglia, in those of the sympathetic system elsewhere, and in the medulla oblongata. None of these is subject to voluntary control, and stimuli arriving through them originate by irritation of the centres directly or by sensory impressions received by these centres. In the latter case it will be seen that a true reflex mechanism is called into play.

Dilatation and contraction of the smaller, peripheral bloodvessels, giving rise to the phenomena of blushing and pallor respectively, are often due to sensory stimulation. This may result as a simple reflex act or with the interposition of an emotional (psychic) state. It may not be unjustifiable to consider the latter as a complex reflex action, as when the sight of an accident happening to another produces pallor, for example. It is also a well-recognized fact that an organ in active functional state is provided with more blood than when quiescent—*i. e.*, relaxation of its vessel walls occurs in the presence of that which excites its function. As an example of this may be cited the stomach; its bloodvessels are comparatively turgid when food is taken, and contracted during a fast.

(*e*) **The Respiratory Tract.**—Mention has already been made of the influence of the blood on the centres of respiration, varying with its degree of oxygenation. It is well known that respiration may not be voluntarily long suspended, the venous blood stimulating to renewed respiratory movements overcoming voluntary inhibition.

Certain volatile gases, as well as odors of certain kinds, stimulate respiration, while others depress it, both acting in a more or less complicated, reflex manner. Here, too, an emotional state may be, as it were, interposed.

c. The Location of Reflex Centres.

A diagram of the various reflex centres corresponding to the reflex actions above mentioned must of necessity include not only the axile motor-cell groups, giving origin to the motor nerves that produce the respective movements, but also the various sensory centres in the same cerebrospinal stem capable of stimulating those motor-cell groups. In the cases of the organic reflexes, as well as in those of many of the superficial reflexes, these sensory centres are very numerous and their connections with the motor centres multiplex. Furthermore, such a diagram could be of little service in diagnosis in the absence of other symptoms, since the loss of any given reflex is not evidence always of disease of either centre, but may be due to a lesion located anywhere in the reflex arc. As an aid, however, to the location of lesions recognized as being in the cerebrospinal stem the following table may be of service:

REFLEX.	LOCATION OF CENTRE.
Plantar.	I. and II. Sacral Segments.
Gluteal.	IV. and V. Lumbar.
Cremasteric.	I.-III. Lumbar.
Erectile of Penis.	I.-II. Lumbar.
Abdominal.	VII.-XI. Dorsal.
Laryngeal.	X. Cranial Nerve. Bulb.
Pharyngeal.	X. Cranial Nerve. Bulb.
Nasal.	V. Cranial Nerve. Bulb.
Conjunctival.	V. Cranial Nerve. Bulb.
Tendo Achillis.	III.-V. Sacral.
Ankle Clonus.	V. Lumbar.
Patellar.	II. Lumbar.
Biceps.	V.-VI. Cervical.
Triceps.	VI. Cervical.
Scapulohumeral.	V. Cervical to I. Dorsal.
Inf. Maxillary.	V Cranial Nerve. Bulb.
Defecation.	IV. Lumbar.
Micturition.	III. Lumbar.
Seminal Emission.	IV. Lumbar to III. Sacral.
Parturition.	I.-II. Lumbar.
Intestinal Movements.	X. Cranial Nerve in Bulb.
Duodenal Regurgitation.	I -V. Dorsal (Splanchnic).
Pylorus.	X. Cranial Nerve in Bulb,

REFLEX.	LOCATION OF CENTRE.
Gastric Movements.	X. Cranial Nerve in Bulb.
Emesis.	X. Cranial Nerve in Bulb.
Deglutition.	X. and XII. Cranial Nerves in Bulb.
Sucking.	V., VII., and XII. Cranial Nerves in Bulb.
Respiration:	Tip of Calamus scriptorius.
Expiration.	X. Cranial Nerve in Bulb.
Inspiration.	X. Cranial Nerve in Bulb.
Circulation:	
Cardiac acceleration.	II.–III. *et seq.*, Dorsal.
Cardiac inhibition.	X. Cranial Nerve in Bulb.
Vasomotor dilatation, *blush.*	VII. Cranial to III. Sacral.
Vasomotor constriction, *pallor.*	II. Dorsal to II. Lumbar, inclusive.
Pupillary.	IV. Cervical to III. Dorsal.
Vasomotor.	Floor of the fourth ventricle.
Salivary secretion.	VII. Cranial Nerve in Bulb. Chorda Tympani.

3. THE SPINAL CORD AS A TROPHIC CENTRE.

In considering the functions of the spinal cord, sight must not be lost of the inherent property of cell bodies here, as, indeed, everywhere throughout the nervous system, to maintain the nutrition of the more distal parts of the respective neurones. The centre of trophic control is apparently vested in the gray matter. Lesions of the anterior horn, since they destroy its motor cells, produce atrophy or dystrophy of the muscles supplied by them. Indeed, as has been shown, atrophy of muscles with flaccid paralysis is one of the signs of disease of the lower motor neurone. Lesions of the posterior horn, and especially of its base, as well as lesions of the intermediate gray matter of Gowers between the ventral and dorsal horns, are frequently attended with trophic cutaneous diseases. Thus transverse myelitis is always associated with decubitus; and trophic ulcers in various locations or trophic disturbances of joints represent a cardinal symptom of syringomyelia, the pathologic changes of which are limited to the gray matter. On the other hand, locomotor ataxia is frequently associated with various arthropathies, and sometimes with perforating ulcer, without appreciable change in the gray matter. Herpes zoster and herpes of the extremities are trophic disturbances due to pathologic changes in the dorsal spinal ganglia. It is not, therefore, possible to select any particular portion of the cord and to ascribe to it the name of trophic centre. Just as the cord, as a whole, is a conductor of impulses upward and downward, so also is it a centre for the control of the nutrition of the trunk, both muscular, cutaneous, osseous, and arthritic.

C. THE PHYSIOLOGY OF THE MEDULLA OBLONGATA AND PONS VAROLII.

Like the spinal cord, the medulla and pons represent a path of communication between the periphery and higher centres for both efferent and afferent impulses, and they also act as independent centres, regulating functions of the utmost importance in the system.

1. THE MEDULLA AND PONS AS A CONDUCTING MEDIUM.

a. The Efferent Pathways.

Those concerning which our knowledge is approximately definite are three in number: the pyramidal tract, the corticopontine-cerebellar tract, and the fasciculus longitudinalis posterior (medialis), commonly spoken of as the posterior longitudinal bundle. There are other efferent pathways, to be sure, particularly the motor speech tract, the cerebral tracts to the motor cranial-nerve nuclei, and certain tracts from the cerebellum to the cord, but our knowledge concerning these is too hazy to be of value.

1. **The Pyramidal Tract.**—The path in the medulla which transmits volitional motor impulses is fairly well understood. For our knowledge of it we are more indebted to the careful study which has been made of secondary degeneration of the medullary tracts and to the phenomena of disease than to any direct experimentation. Direct experiments on the medulla itself are full of difficulties and the results complicated.

That the pyramids are the paths of volitional motor impulse is proved most satisfactorily by the secondary degeneration which ensues in them in consequence of destruction of the cortical motor centres. The pyramid degenerates on the same side as the cortical lesion and as far as the point of decussation of the pyramids, and thence the degeneration is continued downward in the pyramidal tract of the lateral column of the spinal cord on the opposite side and partly also, as will be remembered, in the anterior pyramidal tract of the same side, for a certain distance at least. Experimental evidence as to the result of section of the pyramids is somewhat uncertain, but in monkeys and man there can be no question as to their being the motor paths between the cortex and the anterior horns of the spinal cord.

More or less intimately associated with the pyramidal tract fibres are others from the motor cortex to the nuclei of the motor cranial nerve nuclei in pons and medulla, namely, the motor nuclei of the fifth, sixth, seventh, tenth, eleventh, and twelfth cranial nerves.

Undoubtedly these pathways, at present not clearly defined anatomically, decussate just before reaching their destination, much as the direct pyramidal tract fibres are thought to decussate in the cord just before reaching the particular ventral-horn cells which they are destined to supply. Possibly there is a separate pathway to the facial and hypoglossal nuclei, acting as a motor speech tract, connecting the cortical centre for articulate speech with the medullary and pontine secondary centres, the nuclei of the facial and hypoglossal nerves. Pontine injuries would indicate in some instances such a differentiation.

2. **The Cerebropontine-cerebellar Tract.**—This pathway is composed of two neurones, the upper extending from cerebral cortex to pons, and the lower extending from pons to cerebellum. There are numerous fibres found in the pes pedunculi associated with pyramidal tract fibres coming from the frontal, temporal, and occipital cortex. These fibres are the axones of the cerebrocortical cells. They evidently pass largely in connection with the pyramidal tract to the pons, where they end by arborizing about the cells of the nuclei pontis of the same side. These cells receive the impulse and send them out through their axones, across the midline to the opposite side of the pons, and then upward through the middle cerebellar peduncle (brachium pontis) to the cerebellum. Thus the cerebral cortex of one side is in control of the cerebellar cortex of the opposite side. The nature of the impulse is partly conjectural. It is doubtless true that the volitional motor impulses sent from brain to the opposite side of the spinal cord are not detailed ones, but general ones, since there are no centres for individual muscles in the motor cortex, but centres for combined actions only. It is likely that the cerebrum entrusts the cerebellum with the co-ordination of impulses of volition. At the same instant that the volitional impulses proceed downward to the cord, it is likely that similar impulses proceed to the cerebellum, which organ modifies them, turning them into co-ordinating impulses, and sending them downward to the ventral-horn cells either through the so-called anterolateral descending cerebellar tract of Löwenthal and Marchi, or through the descending root from Deiters' nucleus, or both. Thus the cerebrum controls the opposite side of both cerebellum and cord, and the cerebellum controls the cord of the same side.

3. **The Fasciculus Longitudinalis Posterior.**—The posterior longitudinal bundle is still an anatomic problem, and its function is even more conjectural than its anatomy. It apparently rises in the depths of the thalamencephalon, and has been traced with certainty backward through midbrain, pons, and medulla as far as the upper portion of the cervical cord, where it lies in the anterolateral area, fairly intimately associated with Deiters' tract (tractus acusticospinalis). It appears to receive and to give off short fibres throughout its long

course. That its constituent fibres are short is proved by degeneration experiments on mammals. There is strong evidence that in the lateral portions of the posterior longitudinal bundles are fibres which have decussated in the posterior commissure, and, according to Edinger, numerous fibres within it are derived from a sagittal nucleus in the midbrain, called the nucleus of the posterior longitudinal bundle. The most striking anatomic fact is its intimate relation to the motor nuclei of the ocular cranial nerves pre-eminently, and to the motor nuclei of the seventh and twelfth cranial nerves in the pons and medulla. Into each motor nucleus it sends fibres or collaterals, and from each motor nucleus it receives them. Evidently one of its chief functions is to correlate various eye movements. Fibres also enter the bundle from the auditory system, according to Edinger. The fibres passing to the facial nucleus have been thought by Mendel to supply the orbicularis palpebrarum and corrugator supercilii, so that these muscles may act synergetically with the levator palpebræ superioris supplied by the oculomotor nerve. Possibly, too, the posterior longitudinal bundle co-ordinates the muscles supplied by the seventh and twelfth cranial nerves in speech, thus harmonizing the movements of the orbicularis oris with those of the tongue. Duval and Laborde have described fibres passing upward (*afferent* in direction, therefore) from the nucleus of the abducens nerve to the opposite nucleus oculomotorius, for the supply of the opposite internal rectus muscle. Thus, co-ordination in the simultaneous movement of the external rectus of one side and of the internal rectus of the other is obtained.

It has also been suggested with much plausibility that since movements of the eyeballs are invariably associated with movements in the muscles of expression, and since the fasciculus longitudinalis posterior connects the nuclei of the seventh and twelfth cranial nerves, it is the correlating factor. Since the bundle extends into the upper cervical cord, occupying an area taken up largely with co-ordinating cerebellar fibres, it possibly has something to do with the unconsciously assumed posture of the head when anything is critically examined with the eyes; and the act of listening, attended with special movements of the head, may possibly be functionally associated with the posterior longitudinal bundle, if Edinger's statement that it is connected with the auditory system is correct.

b. The Afferent Pathways.

These consist chiefly of the mesial and lateral fillet.

1. **The Mesial Fillet.**—As was pointed out in the consideration of the spinal cord as a medium of conduction, the mesial fillet apparently conducts all varieties of common sensation. Impulses from the muscles and deep-lying structures, ascending in the dorsal

columns, upon reaching the nuclei gracilis and cuneatus, are transferred through the sensory decussation to the opposite side of the medulla, where they meet the fibres which have already decussated in the cord, and which are conducting upward impulses of touch, temperature, and pain. Thus all of the sensory impulses in the mesial fillet are derived from the opposite side of the body.

Great confusion reigns as to the distribution of the various kinds of sensory impulses among the parts of the fillet. Since the dissociation symptom (preservation of tactile sensation with loss of the thermal and algesic sensations) may be met with in disease of the medulla and pons, it is evident that further physiologic differentiation will some day be forthcoming. Very important is the fact that from the nuclei of the sensory nerves of medulla and pons fibres pass in to the fillet. Thus the sensations brought to pons and medulla by the sensory cranial nerves sweep upward, after immediately decussating, in the contralateral fillet, to the ventrolateral thalamic nucleus, and thence to the cerebral cortex. Thus the fillet is a great river of sensory impulses flowing continuously toward the brain, now and then receiving a tributary from a sensory cranial nerve.

2. **The Lateral Fillet** is made up wholly from fibres of the auditory apparatus. These enter the pons, decussate, become more or less intimately associated with the superior olive, and then ascend in the lateral fillet. The impulses conducted are undoubtedly from the auditory apparatus, and they will be more completely considered when the auditory nerve is mentioned.

(*c*) **Association Pathways.**

Other pathways exist, most of them association paths, the functions of which are obscure. The great system of fibres connecting the olive of one side with the opposite cerebellar hemisphere is still a physiologic problem. Clinical evidence goes to show that it is part of the cerebellar co-ordinating system.

2. THE MEDULLA AND PONS AS AN INDEPENDENT CENTRE.

1. **General Considerations.**—As such they preside over and regulate functions on the due performance of which life essentially depends, as well as many others of considerable complexity, but of less vital importance, All of the cranial nerves with the exception of the first four (viz., the olfactory, optic, motor-oculi, and pathetic) have their primary origin in the medulla and pons; and the third and fourth nerves, though springing from nuclei in the floor of the aqueduct of Sylvius, are also connected with the sixth pair through the posterior longitudinal bundles. Should all the encephalic centres

above the pons and medulla be removed, the mulilated organism, even if a warm-blooded animal, can live and breathe. The functions depending on the spinal centres will go on automatically and under reflex actions will be called forth in the regions innervated. Thus the eyelids will close if the conjunctiva be touched; the lingual, oral, and facial muscles will contract and the ear twitch on irritation of the sensory nerves in reflex relation with the movements in question. The movements capable of being elicited through the medulla are in many instances of remarkable complexity. Thus if a morsel of food be placed on the back of the tongue the combined and co-ordinated movements of the lips, tongue, palate, and pharynx concerned in the mechanism of deglutition will be executed with as great precision as in perfectly normal conditions. In a young animal, so mutilated, the introduction of the nipple between the lips will be sufficient to set up the appropriate movements of sucking.

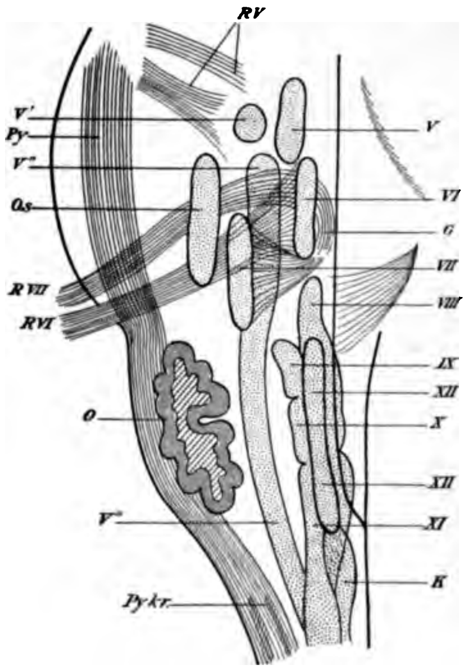
Occasionally human infants are born entirely without cerebral centres above the medulla, and yet an acephalus infant sucks and swallows as well as the perfectly developed child when put to the mother's breast. The medulla is the co-ordinating centre of all these associated movements. Destruction of the medulla causes their instant and permanent annihilation.

The various afferent and efferent nerves concerned in the mechanism, viz., the hypoglossal, glossopharyngeal, facial, and trifacial, all spring directly from gray nuclei in the medulla and pons. Fig. 280 shows the location of the principal nuclei. The plexiform arrangement seen in nerves which are concerned in the movements of the limbs is not manifest in the case of the cranial nerves, except in those of the pharyngeal plexus; but there can be little doubt that there, as in the spinal centres, the nuclei of the various nerves concerned in special physiologic co-ordinations are so connected together that a co-ordinate synergy is occasioned by stimulation just as readily as a single muscular contraction on stimulation of an undivided muscle nerve.

2. **The Lower Speech Centre.**—The movements concerned in the production of articulate speech have their ultimate or lower centre in the pons and medulla, in the nuclei of the seventh and twelfth cranial nerves. This is indicated particularly by the phenomena of disease in this region in man. In bulbar paralysis, the terminal stage of most cases of amyotrophic lateral sclerosis, the disease of the medulla and pons is usually heralded by a slight defect in speech, and the patient has difficulty in pronouncing linguals, labials, and dentals; the voice becomes nasal. The paralysis starts in the tongue and the superior lingual muscle gradually becomes atrophied, so that the mucous membrane is thrown into folds. When the lips later become involved the patient can neither whistle nor pronounce the vowels "o" and "a." Ultimately articulate speech

is entirely lost; the tongue lies a useless, inert, wasted mass in the bottom of the mouth, and saliva constantly drools because the lips are paralyzed. The disease is found to depend upon a process of degeneration affecting the motor nuclei of both medulla and pons. The loss of the power of speech in this disease is a clear demonstration that the lower speech centre is coincident with the nuclei of the facial and hypoglossal nerves. The motor speech tract is doubtless more or less intimately associated with the pyramidal fibres. Undoubtedly they decussate just before their nuclei of destination are reached.

FIG. 280



Schematic transparent section of medulla oblongata, showing the principal centres. The numerals *V* to *XII* refer to the nuclei of origin of the respective cranial nerves. *V* is the motor nucleus; *RV*, the roots of the fifth nerve; *V'*, sensory nucleus; *V''*, sensory nucleus and descending root; *RVI*, root of sixth nerve; *RVII*, root of seventh nerve; *Py*, pyramid; *Pykr*, decussation of the pyramids; *O.s.*, superior olive; *O*, olive; *G.f.*, genu of the facial. (Stewart.)

3. The Cardiac Inhibitory Centre.—It will be recalled that the inhibitory nerves of the heart run in the trunks of the vagi, also that cutting the vagi causes an increase in the number of heart beats; stimulating the cut ends causes a diminution in the number of heart beats. A greater or less degree of inhibition is constantly maintained by the medulla, as is shown by the acceleration of the heart's action which follows section of the vagi. The fibres which cause the inhibition of the heart spring from the spinal accessory nucleus and belong to the motor or centrifugal system. The accelerator nerves of the heart travel through the last cervical and first dorsal ganglia of the sympathetic. Stimulation of these nerves, as has been proved by Gaskell, increases the strength as well as the rate of the cardiac contractions. Very interesting as bearing upon the cardiac inhibitory centre is one of Edinger's cases.[1] He observed pronounced slowing of the pulse on defecation due to the existence of a varix in the anterior portion of the accessorius nucleus. Subsequently, as the varix grew the retardation of the pulse became greater until the heart ceased to beat altogether when the varix ruptured.

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[1] Berliner klinische Wochenschrift, 1898.

The rhythmic movements of the heart are independent of the medulla and of the cerebrospinal centres in general, and are conditioned mainly by the intrinsic ganglia of the heart itself; the heart contracts rhythmically on stimulation apart from all nerves or ganglia.

4. **The Vasomotor Centre.**—The medulla and pons also exert a controlling influence upon the state of the blood pressure. The arterial walls are maintained in a continual state of tone which varies within certain limits, either automatically or in response to reflex action, due to certain local or general afferent stimuli. The tone of the bloodvessels is in a large measure dependent upon the gray matter of the spinal cord, the various segments of which may be regarded as more or less independent *vasomotor centres.* But the predominating influence in the vascular system and the presiding influence over the variations in the blood pressure depend upon the centre in the medulla. As long as the medulla and pons are intact, all the centres situated above it may be removed without greatly influencing the tone of the bloodvessels or interfering with the variations of blood pressure. If, however, the cord be severed below the calamus scriptorius a general vasomotor paralysis ensues with enormous fall of blood pressure, owing to the greatly increased vascular area. More precisely the centre corresponds to the ganglionic cells of the upper olive or the anterolateral nucleus of the medulla. This region, or its homologue in other animals, is termed the vasomotor centre, and this centre is supposed to be connected with all the afferent nerves capable of modifying its influence. Stimulation of the sensory nerves causes an excitation of the vasomotor centre and constriction of the arteries.

5. **The Vomiting Centre.**—Irritation of the branches of the vagus nerve distributed to the alimentary canal induces vomiting, in which there is a combination of movements. The essentials are dilatation of the cardiac orifice of the stomach, and forcible pressure on this viscus by the expiratory muscles of the abdomen. It is customary to consider a special vomiting centre, which is supposed to co-ordinate all these movements, but it is now held by physiologists that the facts do not justify a centre distinct from the respiratory centre, with such modifications as are conditioned by the starting point of the exciting stimulus.

6. **The Respiratory Centre.**—The co-ordination of the respiratory movements is one of the most important functions of the medulla oblongata. As long as the medulla is intact the function of respiration goes on in an automatic or reflex manner with perfect regularity and rhythm. When the medulla is destroyed respiration ceases and

death ensues in all animals which cannot live by cutaneous respiration alone, like the frog. The chief centre of co-ordination of the respiratory movements is situated near the beak of the calamus scriptorius, coinciding, or being in the closest relation, with the nuclei of the vagus nerves. From this point proceed the impulses which excite the associated and co-ordinated movements of the diaphragm, thoracic walls, and air passages.

If the spinal cord be cut above the origin of the phrenic nerve, the thoracic muscles and diaphragm speedily cease to act effectively for purposes of respiration, but, as it has been shown, may still continue to act rhythmically and to respond to stimulation of certain sensory surfaces for a short period after section of the cord below the calamus. In some animals respiratory movements continue for a longer or shorter period after complete removal of the medulla oblongata. The respiratory centre is in reality not a single-cell group, but a bilateral group, each in relation to the vagus centre of its own side. The two act normally in perfect unison, but they may be divided by a longitudinal incision in the median line, and then they lose their absolute synchrony, and each half of the respiratory apparatus performs its function independently of the other. The respiratory centres are in relation, not only with the afferent impressions conveyed by the vagus, but also with those of the sensory nerves in general, and very manifestly with those of the head and chest. Hence a sudden stimulation of these surfaces, such as by a dash of water, may cause active inspiratory movements; or if very severe, it may cause spasmodic arrest for a time, either in a state of inspiration or, under certain circumstances, of expiration.

The rhythmic alteration of inspiratory movements is not, however, entirely dependent on reflex excitation, for respiratory movements may continue after all the afferent nerves connected with the centre have been divided. In this case there is a true automatic activity influenced by the state of the blood itself. The diminution of oxygen and accumulation of oxidation products in the blood act as a stimulus to the respiratory centres. When the blood is artificially hyperoxygenated the movements of respiration come to complete standstill, a condition termed apnœa. Non-aeration of the blood, resulting from obstruction of the respiratory functions, powerfully excites the movements of both inspiration and expiration, and ultimately, if the obstruction continues, causes general convulsions of the whole body, as in asphyxia.

The respiratory mechanism, though essentially automatic or reflex, is to a great extent under the control of the will. It is by the volitional control we possess over the respiratory movements that we are enabled to combine them with those of articulation for the purpose of speech and vocalization, and in a similar manner by closure of the glottis and forcible contraction of the expiratory muscles we can aid the expulsion of the contents of rectum and genitourinary organs. Our volitional control over the respiratory mechanism is limited. No one by mere will power can inhibit his respiration long enough to produce death.

7. **The Taste Centre of the Medulla.**—According to Edinger the long, thin column of gray matter to the mesial side of the fasciculus solitarius and known as the nucleus fasciculi solitarii is the medullary or lower taste centre, and to the cells of this nucleus pass fibres which come from the dorsum linguæ, partly by way of the gustatory branch of the trigeminal nerve, partly by way of the chorda tympani, through the facial, large superficial petrosal, Vidian, sphenopalatine, superior maxillary and trigeminal nerves, and partly by way of the glossopharyngeal. Wallenberg succeeded in tracing to this nucleus taste fibres from the entering trigeminal roots. The taste impulses, having been received by the cell bodies of the nucleus, pass out by way of their axones, decussate, and probably ascend in the contralateral fillet.

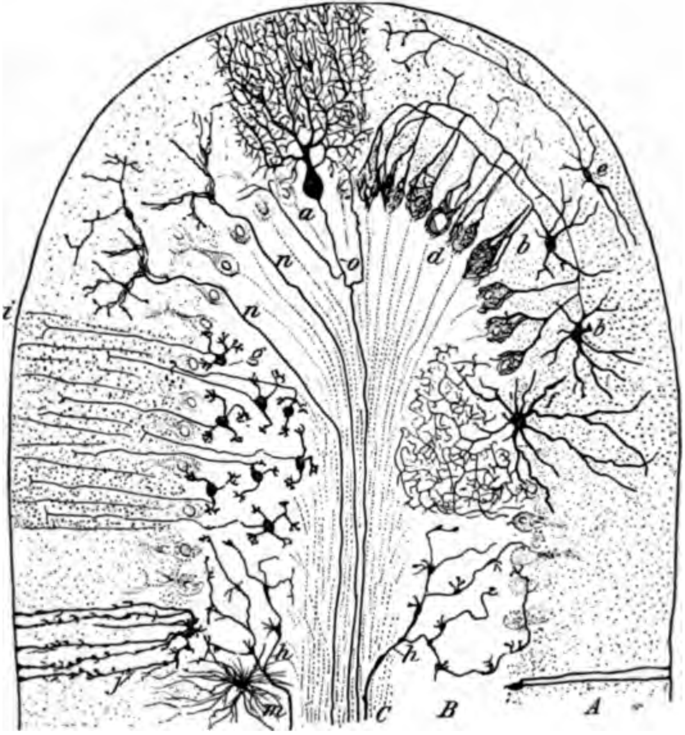
8. **The Medulla Oblongata is a Co-ordinating Centre of Reflex Actions Essential to the Maintenance of Life.**—If all the centres above the medulla oblongata be removed, life may nevertheless continue. The respiratory movements may go on with their accustomed regularity and rhythm; the heart will continue to beat and the circulation be regulated as under normal conditions; the animal may swallow food if it be placed in its mouth, may react in apparently purposive manner to impressions made on the sensory nerves, withdrawing its limbs or endeavoring to remove itself from the cause of irritation, or even utter a cry of pain, and yet will be merely an unconscious, unintelligent reflex mechanism.

D. CO-ORDINATION AND EQUILIBRATION; THE PHYSIOLOGY OF THE CEREBELLUM OR METENCEPHALON.

1. CO-ORDINATION: ADJUSTMENT OF MUSCULAR ACTION.

To the most casual observer the necessity of a correlating influence in muscular movements must be apparent, an arrangement by which any change in position of a part of the body is accomplished through a nicely opposed action of two or more sets of muscles. Of these one relaxes as the other contracts, or, where several groups are concerned, different degrees of change in tension occur in the different groups, to just the extent necessary to produce the desired movement. Such a force must be efferent—*i. e.*, exerted on the motor cells in the ventral horn of the spinal cord. Moreover, the centre from which it rises must be in intimate relationship with those afferent nerve currents through which, either as general or as special sensation, we recognize our position relative to our surroundings. Such afferent impulses in all probability arrive through all the varied sense apparatus, as may be learned when one or more is wanting. This *centre of unconscious control of muscular movement* determined by unperceived sensation, so to speak, *is the cerebellum.* The controlling force which it exercises is co-ordination. Through its peduncles connecting its hemispheres with the cerebrum, with the medulla and cord, and with each other, it receives afferent impulses and emits efferent ones. (See Fig. 281.)

Fig. 281



Semidiagrammatic transverse section of a cerebellar convolution of a mammal: *A*, molecular layer; *B*, granular layer; *C*, zone of the white substance; *a*, cell of Purkinje; *b*, small star-shaped cell of the molecular layer; *d*, terminal descending arborizations surrounding the cells of Purkinje; *e*, superficial star-shaped cells; *f*, large star-shaped cells of the granular layer; *g*, granules with their ascending axis cylinders bifurcated at *i*; *h*, mossy fibres; *j*, neuroglia cell with plume; *m*, neuroglia cell of the granular layer; *n*, climbing fibres; *o*, ascending collaterals of the axis cylinders of the Purkinje cells. (Cajal.)

Though there is a more general agreement among physiologists as to the results of lesions of the cerebellum than of any other portion of the encephalon, there seems to be a correspondingly greater difficulty in finding such a definition of the functions of this organ as shall have a clinical and physiologic value. Experiments prove satisfactorily that destruction of the cerebellum in the lower animals is followed by long-continued, if not permanent, disorders of co-ordination, especially of that great subdivision of co-ordination which we call equilibration.

The cerebellum does not respond to mechanical irritation in the same way that the cerebrum responds; extensive co-ordinated movement-complexes take place rather than comparatively simple ones. It has been found, for example, that if the induced current be applied to the cortex of the cerebellum in rabbits a series of ocular and other movements occur, depending upon the point which is stimulated. Electric stimulation of the cerebellum produces simultaneous movements of both eyes in different directions, according as the electrode is applied to different parts of its surface. Besides these ocular movements, certain movements of the head and limbs are likewise produced. In some experiments in which the head was maintained in a fixed position, only movements of the eyes and also sometimes of the limbs could be observed, but when the head was released the movements of the eyes coincided with movements of the head. Along with these effects the pupils were observed to become contracted on irritating the cerebellum. The contraction of the pupil is specially marked on the eye of the same side. The pupil may remain contracted for some time after the electric current has been removed.

Injuries to the cerebellum or to the cerebellospinal pathways cause a peculiar disorder of co-ordination named *diadocokinesia* by Babinski[1] who discovered it. He noted that in patients with cerebellar lesions, whereas pronation and supination each by itself could be readily executed, the alternation of the two acts required twice or three times as much time as in a normal individual. The essence of the disturbance is an inability instantly to arrest one motor impulse and to substitute another diametrically opposite. There is, then, a special co-ordinating function of the cerebellum, which consists in the instantaneous association of an excitomotor impulse with a mental action. Volitional acts to be perfect require the integrity of this function. It is indispensable in walking, for this requires instantaneous sequence of action in opposing muscles. It is seen in the writing of a cerebellar patient, the curves being poorly formed and broken, owing to impairment of this function.

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[1] Revue neurologique, November 15, 1902.

2. EQUILIBRATION: CO-ORDINATION OF MOVEMENTS MAINTAINING EQUILIBRIUM.

The cerebellum seems to be a complex arrangement of individual, differentiated centres which in associated action regulate the various muscular adjustments necessary to maintain equilibrium and steadiness of the body. We should therefore expect to find that a lesion which annihilates the functional activity of any of the individual cerebellar centres should manifest itself in a tendency to the overthrow of the balance in the direction naturally opposed by this centre. This is in accordance with the facts of experiments. Stimulation of the anterior part of the middle lobe excites muscular combinations which would counteract a tendency to fall forward. Hence destruction of this part shows itself in a tendency to fall forward. In this we see both the negative effect caused by the removal of the one centre, and the positive effects excited by the unopposed and antagonistic centres. In a like manner stimulation of the posterior part of the middle lobe calls into play the muscular adjustments necessary to counteract a backward displacement of the equilibrium; and a destruction of this region manifests itself in a tendency to fall backward.

The lateral lobes of the cerebellum contain centres for complex adjustments against lateral, combined with diagonal and rotary, displacements to the opposite side, and hence, as has been found by experiments, lesions of the lateral lobes exhibit themselves in disturbances of the equilibrium either laterally to the side opposite the lesion or, as the resultant of lateral and rotary displacement, in rolling over to the side of the lesion. The effects of a lesion may therefore vary—a fact which may account for some of the discrepancies among the results obtained by different experimenters.

The mechanism of cerebellar co-ordination is not wholly independent of consciousness and volition. The displacement of equilibrium in any direction not only calls into play by reflex or responsive action the compensatory motor adjustments, but also induces conscious or voluntary efforts of a similar or antagonistic, compensatory nature. Thus a tendency to fall forward, while reflexly calling into action the muscular combinations which pull the body backward, may also excite consciousness and cause voluntary effort in the same direction. The same muscular adjustments which are capable of being effected by the cerebellum are also under the control of the will and may be carried out by the cerebral hemispheres independently of the cerebellum; nevertheless, an animal deprived of its *cerebral* hemispheres is capable, by means of its cerebellum, not only of maintaining its equilibrium if undisturbed, but of regaining it when overthrown. Conscious cerebral control of equilibrium is, therefore, merely supplementary to cerebellar control.

The disturbance of equilibrium is always most marked immediately after the infliction of injury to the cerebellum. This, which has been by many looked upon as a sign of irritation, is to be accounted for by the sudden derangement of the self-adjusting mechanism on which the maintenance of equilibrium mainly depends. As, however, the animal may supplement the loss of this mechanism by conscious efforts, in process of time it acquires the power of voluntary adaptation and thus is enabled to maintain its equilibrium, though perhaps with less degree of security than before.

The more extensive the lesions the greater the disturbance of the mechanism and the greater the difficulty of effecting through conscious effort all the muscular adjustments necessary to maintain the balance. The disturbances of equilibrium are, therefore, of a more enduring character, and it is only by a long process of training that volitional accommodation replaces a mechanism essentially independent of consciousness. Even should this point be reached, the constant attention necessary to preserve steadiness of movement and prevent displacement of equilibrium would be a heavy strain on the animal's power; and it would be in accordance with this condition that prolonged or varied muscular exertion should cause great apparent exhaustion, actually verified by experiments on animals.

a. Relation between Cerebellar Development and Equilibratory Power.

Every form of active muscular exertion necessitates the simultaneous co-operation of an immense assemblage of muscular movements throughout the body to secure steadiness and maintain the general equilibrium; and on the hypothesis that the cerebellum is the centre of these unconscious adjustments, we should expect the cerebellum to be developed in proportion to the variety and complexity of the motor activities of which the animal is capable. The facts of comparative anatomy and development are entirely in harmony with this hypothesis. In the reptiles and amphibia, whose movements are groveling and sluggish or of the simplest combination, the cerebellum is of the most rudimentary character, while in mammals it is richly laminated and the lateral lobes highly developed in proportion to the motor capabilities, represented in the motor zone of the cerebral hemispheres.

If we compare the relative development of the cerebellum in the several orders of the same class of animals we find it highest in those which have the most active and varied motor capacities, irrespective of the grade of organization otherwise; and the cerebellum of the adult is, relatively to the cerebrum, much more highly developed than that of the newborn infant, a relation which evidently coincides with the growth and development of the muscular system.

b. The Maintenance of Equilibrium.

This involves the conjoint operation of three separate factors: (I) A system of afferent nerves and organs. (II) A co-ordinating centre. (III) Efferent tracts in connection with the muscular apparatus concerned in the action. The faculty of equilibration is overthrown by lesions of the afferent apparatus alone or by lesions of the co-ordinating centre alone, or by lesions of the efferent tract alone, or by conjoint lesions of all. Various degrees and forms of disturbance of this function will result, according to the nature, extent, and position of the lesion. In many respects the maintenance of the equilibrium resembles the tone of the muscles. Lesions of the afferent nerves, central ganglia, or motor nerves destroy the tone of muscles, and according as this occurs in both or only in one group of antagonistic muscles we have complete muscular flaccidity, flexion, or distortion. So in regard to equilibrium, similar lesions may cause complete overthrow, or various forms of distortion such as reeling, staggering, rotation, etc.

1. **The Afferent Apparatus.**—The co-ordinating centre or cerebellum apparently derives its data for equilibration from four main sources. These four systems of sources are: (I) Organs for the reception and transmission of muscular sense impulses. (II) Organs for the reception and transmission of tactile impressions. (III) Organs for the reception and transmission of visual impression. (IV) The semicircular canals of the internal ear, and their afferent nerves. Each of these systems will be considered separately.

(*a*) **The Influence of Muscular Sense Impulses.**—The importance of a proper conduction of impulses to the cerebellum is extremely well illustrated in those cases of spinal-cord disease in which the direct cerebellar tract is injured. For example, in the disease known as hereditary cerebellar ataxia, where the ataxia is unquestionably exquisitely cerebellar in type, the chief lesions are found not in the cerebellum, but in the spinal cord, in the fibres which conduct muscle and joint sensory impulses to the cerebellum. The cerebellum thus directly derives a vast amount of information from the muscles, joints, bones, and deep-lying structures, particularly concerning their absolute position, and also concerning their position with reference to other structures. These impulses are conducted to the cerebellum by the direct cerebellar tract through the corpus restiforme to the hemisphere of the same side, or by way of the anterolateral ascending cerebellar tract of Gowers through the superior cerebellar peduncle.

The cerebellum doubtless also derives information of this character by another pathway. It is known, for example, as has already been pointed out, that the columns of Goll and Burdach, which carry muscle and joint sensory impulses to the cerebral hemispheres by way of the cells of the nucleus gracilis and cuneatus through the mesial fillet, transfer *some* of these impulses to the cerebellum from those nuclei by way of the dorsal external arcuate fibres which ascend through the corpus restiforme of the same side to the cerebellar hemisphere. The olivary bodies are also undoubtedly concerned in some manner with the conduction of these impulses (although the anatomic pathway is at present vaguely understood), because if they be injured disturbances of equilibrium result, with rolling, forced movements, and deviation of the optic axes similar to those caused by lesions of the middle cerebellar peduncles. Since all of these spinal cerebellar pathways, except Gowers' tract, and since the olivary cerebellar pathways all pass to the cerebellum by way of the corpus restiforme, lesions of the latter should give cerebellar symptoms. If they are examined for the purpose of ascertaining this point, it will be found that most turbulent disorders of co-ordination and equilibration follow, so closely resembling those of lesions of the cerebellum itself as to make a differential diagnosis extremely difficult.

(*b*) **The Influence of Tactile Impressions.**—A frog deprived of its cerebral hemispheres, but in which the optic lobes and cerebellum are intact, still preserves the power of maintaining its equilibrium. If now the skin be removed from the hinder extremities the animal at once loses this power, and falls like a log when the basis of support is tilted. The removal of the skin has destroyed the receptive organs of those sensory impressions which are necessary to excite the co-ordinating centre so that the various combinations of muscles shall maintain the animal in equilibrium. It is a law laid down by Volkmann, and verified by all subsequent observers, that reflex reactions are more capable of being excited by impressions on the peripheral extremities of afferent nerves than by stimuli applied to any other part of their course. A similar result ensues in man, as has been shown by Heyd when the soles of the feet are rendered insensible by chloroform or refrigeration. The individual experiences great difficulty in maintaining equilibrium when further embarrassed by shutting his eyes, and he oscillates and sways in a very pronounced manner. In locomotor ataxia the same oscillation is observed, and it is due, in part, to the same cause. In this disease there is frequently, among other symptoms, diminution or absence of sensibility to tactile impressions in the feet, so that the patient feels as if something soft were interposed between them and the ground, or he does not feel the ground at all. The impairment or abolition of tactile sensibility is capable of being compensated for, up to a certain point at least, by visual and other forces, but when the eyes are shut, or the light withdrawn, equilibrium becomes difficult or impossible.

On the whole the influence of such tactile impressions, while important, is much less than the influence of visual impressions in the preservation of the equilibrium; for even a normal individual who stands with his feet close together and his eyes closed perceives more or less oscillation.

The pathway by which tactile impressions reach the cerebellum is obscure. Possibly they leave the fillet by way of the ventral external arcuate fibres, which arborize about the cells of the nucleus arcuatus. The axones of these cells then proceed up the corpus restiforme into the cerebellum. The whole matter, however, must be admitted to be at present speculative. It is evident that the evidence must be wholly anatomic and not physiologic, because we are not conscious of the impulses which go to the cerebellum. Therefore, even though a large tract of fibres conveying tactile impulses should pass into the cerebellum by the corpus restiforme, lesions of the latter could produce absolutely no subjective tactile losses on the part of the individual. That the cerebellum *must* receive tactile impulses concerned in the maintenance of equilibration is proved by the frog experiment mentioned in the beginning of the first paragraph on this subject.

(*c*) **The Influence of Visual Impressions.**—Equilibration and motor co-ordination may be acquired in the first instance and exercised without the aid of the eyes, as exemplified in those born blind. But in general the motor adjustments used in regulating equilibrium are guided by the sense of sight. The child who learns to walk keeps his eyes continually on his limbs and the surrounding objects, and sees that his movements are made in accordance with the end desired.

When the movements become organized and automatic by frequent repetition the guidance of the eyes ceases to be so necessary; and the impressions, conditioned by the movements themselves, are sufficient to ensure the requisite simultaneous and successive motor adjustments. But even then visual impressions, though not closely affecting consciousness, are not inoperative, as is proved by the uncertain and wavering character of motor adjustments, even of the most habitual or automatic character, when the eyes are shut or the light withdrawn. When there is defect or total default of tactile sensibility, equilibration is impossible, except with the aid of vision. The sense of sight may compensate for a total absence of tactile (including muscular) sensibility, and an individual who has no sensibility in his lower extremities, and who falls like a log when he shuts his eyes, may stand or walk if he looks at his feet. This, however, always implies strained effort and speedily induces fatigue.

It would seem that the act of keeping the eyes open is of itself an aid to equilibration, though the eyes are useless as organs of vision. It has been observed that patients suffering from locomotor ataxia who were entirely blind before acquiring that disease, and able to stand with their eyes open, oscillate much more when they are shut. This is probably due to the interruption of the act of fixed attention, of which the steady gaze, even with sightless orbs, is the physical expression.

The influence of vision on equilibration is further shown in the disturbances created by unusual movements in the field of vision, either by movements of the objects themselves, or induced by faults in the oculomotor apparatus. We associate position in space, not only with certain tactile sensations, but with a certain definite relation to surrounding objects. When the whole field of vision is in motion, or the positions of familiar objects are distorted by obliquity of the optic axis, there is a disturbance of the customary relations between the visual and tactile sensations and a distressing sense of insecurity results—the individual not being able to discriminate clearly whether he himself or the objects around him are in motion or displaced. The difficulty of equilibration under such circumstances gives rise to the sense of vertigo, which is merely the subjective side of the physiologic disturbance. Oscillation of the eyeballs or nystagmus, or the occurrence of paralysis in one of the ocular muscles, such as the external rectus, is a familiar cause of the vertigo which is caused by a lack of harmony between the visual and tactile experiences and associations of our relations to surrounding objects. It was long ago found by Cyon that pigeons are similarly affected by distortion of the optic axis. On placing prisms before their eyes he observed marked disorder of equilibrium amounting, in some cases, to actual falling down.

The course of the pathway taken by visual impulses toward the cerebellum is very uncertain. It is well known, however, in accordance with the teachings of Edinger and others, that fibres proceed from the corpora quadrigemina anteriora backward, decussating, and passing through the superior cerebellar peduncle to the cerebellum; for when the latter are sectioned fibres of degeneration are to be found upon the cerebellar side of the severed peduncle.

A speculative digression at this point may not be amiss. The cerebellum is in our present knowledge an undifferentiated organ, injury of any part of which alike causes cerebellar ataxia. It is even stated by clinicians that one portion of the cerebellum may act vicariously for another. Is it not equally probable that the cerebellar cortex is highly differentiated; that one area receives muscle and joint sense impulses from one side of the body, and a bilaterally symmetric area receives impulses of the same nature from the opposite side; that certain areas are for the reception of impulses of touch very necessary for preservation of equilibrium; that other areas are devoted to the reception of visual impulses, still others to labyrinthine impressions? If such were the case, physiologic experiment, since it could give information of an objective nature only, would be utterly useless in mapping out the cerebellar cortex, since but one symptom would be produced, cerebellar ataxia and vertigo. Such a view of the cerebellum, even though hypothetic, is vastly superior to the one which by analogy we know must be false, namely, that the cerebellar cortex is undifferentiated; and such a view indicates that the anatomist, by mapping the afferent tracts accurately, will be the first to indicate the functional differentiation of the cerebellar cortex.

(*d*) **The Influence of Labyrinthine Impressions.**—The relation between the cerebellum and the auditory nerve is suggested by anatomic considerations. The so-called auditory nerve ought to be subdivided into the vestibular nerve, or nerve of tonus, co-ordination, and equilibration, and the cochlear nerve, or nerve of hearing, just as in times past the seventh nerve of Willis became generally known as the facial nerve and the auditory nerve. The vestibular nerve passes from the ampullæ of the semicircular canals partly to the dorsal auditory nucleus, and partly to the cerebellum, perhaps directly, by way of Edinger's direct sensory cerebellar tract in the inner division of the corpus restiforme. This dorsal auditory nucleus is further connected on the one hand with the superior olive, having connections with the posterior quadrigeminal bodies, and on the other hand with the cerebellum. Further than this almost nothing is known of the central path of the nerve. The cochlear division of the auditory nerve seems to have nothing to do with the cerebellum physiologically, because lesions of the cerebellum do not impair the sense of hearing in animals, nor do diseases of the cerebellum in man cause deafness, except in such cases as lead to direct implication by means of pressure or otherwise of the cochlear division of the auditory nerve or the ventral auditory nucleus.

There is thus an important influence exerted by the semicircular canals upon the function of equilibration, and we have just noted the anatomic foundation for this influence in the connections which exist between the labyrinth and the cerebellum. There is, further, a remarkable and significant similarity between lesions of the individual semicircular canals and injury of certain regions of the cerebellum, and also between direct irritation of the canals and electric irritation of different portions of the cerebellar cortex. Experiments involving the local irritation of the labyrinth in man have led to an hypothesis which assumes that stimulation of the superior vertical canal causes phenomena similar to those produced by irritation of the posterior cerebellar centres; stimulation of the posterior vertical canal, phenomena similar to those produced by irritation of the anterior cerebellar centres; and stimulation of the horizontal canal, phenomena similar to those produced by irritation of the lateral cerebellar centres.

Various forms of irritation applied to the semicircular canals also bring out ocular movements and movements of the head and body exactly like those produced by stimulation of various portions of the cerebellum. Similarly, if air or liquids be injected into the ear of man where the membrana tympani has been ruptured, the eyes turn to right or left, depending upon the side which is injected, and a feeling of vertigo occurs. According to the observations of Flourens and Cyon on pigeons, when the horizontal canal is divided on the side, the head is thrown into a series of oscillations in a horizontal plane around the vertical axis. When the posterior vertical canals are divided the disturbance of equilibration is of a similar character, but more violent. In this case the movements of the head are in a vertical plane around a horizontal axis. Section of the posterior vertical canals causes movements of the head from behind forward and from right to left, or *vice versa*. There is profound disturbance of equilibration and the animal tends continually to turn somersaults heels over head. The plane of the movements of the head in this case is diagonally around a horizontal axis. Thus, analysis of the movements consequent on section of the respective canals shows that they take place in the plane of the canals operated on.

It has been observed that the disturbances of equilibrium after section of one or more of the canals on one or both sides are of comparatively short duration. When the whole of the semicircular canals on one side are destroyed the disturbances of equilibrium are also transitory. When all the canals are destroyed on both sides the disturbances of equilibration are of the most pronounced character. Goltz describes a pigeon so treated, which always kept its head with the occiput touching the breast, the vertex directed downward with the right eye looking to the left, and the left looking to the right, the head being almost incessantly swung in this position in a pendulum-like manner. Cyon says it is impossible to give an idea of the perpetual movements to which the animal is subject. It can neither stand, nor lie still, nor fly, nor maintain any fixed attitude. It executes violent somersaults, now forward, now backward, rolls round and round, or springs in the air and falls back to recommence anew. It is necessary to envelop the animals in some soft covering to prevent their dashing themselves to pieces by the violence of their movements, and even this is not always successful. The extreme agitation is manifest only during the first few days following the operation, and the animal may then be set free without danger, but is still unable to stand or walk, and tumultuous movements come on from the slightest disturbances.

The phenomena observed in connection with lesion of the semicircular canals clearly point to these organs as the source of impressions which are necessary for the maintenance of the equilibrium, and without which optic and tactile impressions alone barely suffice even after prolonged education.

LOCOMOTION.—Animals deprived of their cerebral hemispheres are not only able to maintain their equilibrium, but are also capable of co-ordinated locomotion in their usual manner. Locomotion involves a vast complexity of motor adjustments of the head, trunk, and limbs, beyond the simple combinations of the muscles of the limbs which are co-ordinated in the spinal cord. The centre of gravity is continually varying with each movement of the limbs; this necessitates perpetual readjustment of the trunk and limbs. By stimulation of the spinal cord below the calamus scriptorius the limbs of rabbits, as shown by Ludwig, may be thrown into co-ordinated and alternating actions, such as running and leaping, but the spinal centres alone are unable to provide for the execution of these movements. These require the presence and activity of the mesencephalic and cerebellar centres. When one learns to execute movements, the sense of vision aids in a large measure in directing the body and limbs to carry out the end desired, and one is guided also by the sensations and impressions arising in connection with muscular

FIG. 282

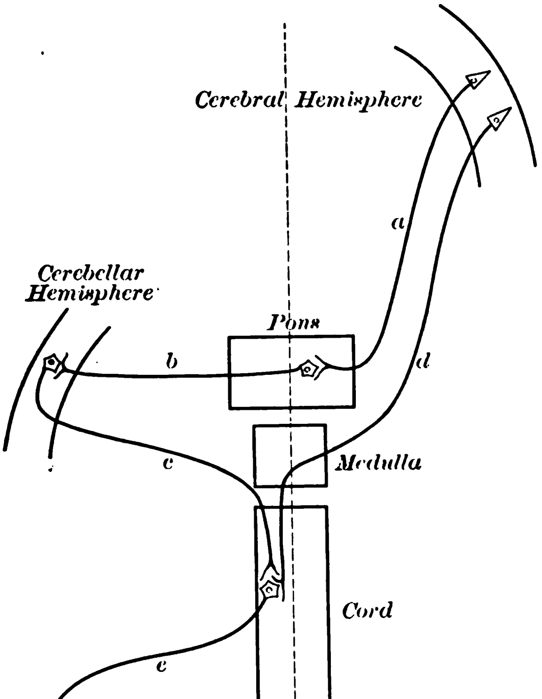


Diagram showing mutual relations of the cerebral hemisphere, cerebellar hemisphere, and spinal cord: *a*, corticopontine neurone; *b*, pontine-cerebellar neurone; *c*, cerebellospinalis neurone; *d*, pyramidal fibre, decussating in medulla; *e*, motor cells of anterior horn of the spinal cord.

action. When these movements have been learned neither vision nor the sense of muscular action seems necessary and the most complex co-ordinations can be executed with precision without attention or consciousness. What has at one time required a conscious effort becomes an organized reflex, provided for in the mechanism of the lower centres.

2. **The Co-ordinating Centre.**—From what has been already said it is very evident that the cerebellum is the co-ordinating centre; and it is equally evident that the centre is one which does not function uniformly throughout its cortex, but is one in which there is division of labor in the same manner that there is in the cerebral hemisphere.

3. **The Efferent Mechanism** is imperfectly known as yet. In treating the cord as a conductor of descending cerebellar impulses, the statement was made that the pathway taken by them was down the anterolateral descending cerebellar path of Löwenthal and Marchi, or else down Deiters' tract (tractus acusticospinalis), or else down both of them. These paths run in the anterolateral area of the spinal cord and end by arborizing about the motor cells of the ventral horn, these latter being also under the stimulating influence of the pyramidal fibres. The mechanism of action is indicated in Fig. 282, which shows how, from the cerebral cortex, the cortico-pontine-cerebellar spinal tract on the one hand and the cortico-spinal or pyramidal tract on the other hand arrive at the same ventral motor cell. Thus with the volitional impulse the co-ordinating impulse is simultaneously delivered.

c. Pathologic Physiology of Equilibration.

Tumors of the cerebellum give rise to symptoms which throw a great deal of light upon the functions of the cerebellum, and the experimentalists, especially Luciani and Thomas, have done much in establishing cerebellar symptomatology. The cerebellum plays both a static and a dynamic part, interference with the former function entailing disturbance of equilibration, both standing and walking; and interference with the latter entailing asthenia and atonia. There are, then, three cardinal symptoms of cerebellar lesions in general: (I) *asthenia*, diminution in the energy of contractions; (II) *atonia*, flaccidity of the muscles; and (III) *astasia*, disturbance of the equilibratory function. This latter symptom has been hitherto more or less confused under the general terms of cerebellar ataxia and cerebellar asynergy.

1. **Astasia.**—Disturbance of the equilibratory function leads to a peculiar reeling, drunken man's gait, vertigo being the leading feature. The patient stands with legs far apart upon a broad base of support, the head and body inclined toward the side of the lesion if the latter is irritative, and the legs trembling more or less violently.

If he walks he turns to the side toward which the body is arched; he therefore cannot walk a straight line, but instead festoons along. There is a marked tendency to fall toward the side of the lesion, though there are some exceptions to the rule. Though common usage has sanctioned the term "cerebellar ataxia," there is no real ataxia; it is merely a loss of co-ordination. Indeed, it is likely that it depends in part or largely upon a loss of the faculty of rapidly associating various movements, a kind of cerebellar asynergy, already referred to as diadocokinesia.

2. **Atonia.**—The atonia is betrayed by the patient's posture in the upright position. There is flaccidity to the point of complete loss of tonus on the side of the body which is the seat of the destructive cerebellar lesion; consequently, the body is arched to the opposite side and the spinal column is curved (skoliosis). If the lesion be irritative there is increased tonus on the diseased side, and the body is arched with the convexity away from the side of the lesion. To Luciani the credit of elucidating this symptom is very largely due. It is splendid proof that the preservation of tonus is an important function of the cerebellum.

3. **Asthenia.**—There is usually present in cerebellar lesions a marked asthenia, frequently so much so as to suggest paresis or paralysis, the patient being unable to execute certain movements, to walk, or even to stand. If the patient attempts to walk exhaustion rapidly follows, and he falls unless supported. The weakness, as a rule, is associated with violent trembling of the legs. Not only is there asthenia of the lower extremities, the upper are also involved. The arms and hands tremble violently; they are unskilful, clumsy, especially in voluntary movements. These disturbances sometimes have a choreic appearance, or are suggestive of the intention tremor of multiple sclerosis. The arms are asthenic, weak, and rapidly tire. The early fatigue is perhaps due to the fact that the cerebral hemispheres, acting vicariously as a co-ordinating mechanism, rapidly become exhausted. Even the speech is affected, scanning and delayed enunciation having been noted.

E. THE PHYSIOLOGY OF THE MESENCEPHALON.

The fully developed mesencephalon is neither an anatomic nor a physiologic unit. It has, therefore, no single function; its functions are rather those of its constituent parts. Of these the most important are: (I) the posterior quadrigeminal bodies; (II) the anterior quadrigeminal bodies; (III) the cerebellocerebral pathway; (IV) the nuclei of the third and fourth cranial nerves; (V) the pes pedunculi.

a. Normal Physiology.

1. **The Posterior Quadrigeminal Bodies.**—The fibrous connections of these bodies are with the lateral fillet and the cortex of the temporal lobe. The fibres of the lateral fillet come wholly from the nuclei of termination of the cochlear nerve or the nerve of hearing; and the accompanying diagram from Edinger (Fig. 283), showing the detailed anatomy of the cochlear nerve, excellently illustrates the mutual relationships between the nerve of hearing, the posterior quadrigeminal bodies, and the temporal auditory cortex.

The posterior corpora quadrigemina, viewed superficially, are apparently related through their corresponding brachia to the visual apparatus, but it is most improbable that they contain fibres which are used in vision. This is more evident because, when the eyeball is extirpated in a young animal, the posterior corpus quadrigeminum remains unaffected.

FIG. 283

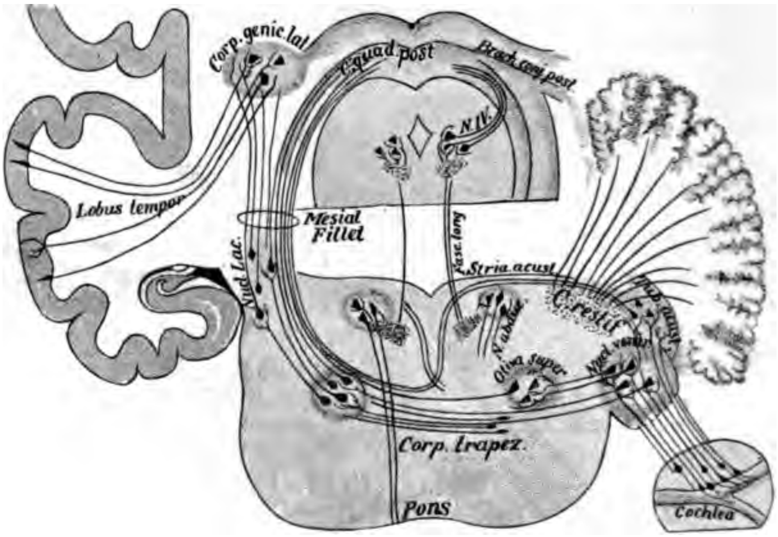


Diagram of the course of the cochlear nerve. The abbreviations are the customary ones. (Edinger.)

The chief function of the posterior quadrigeminal bodies is closely related to hearing. This is indicated by their fibrous connections with the cochlear nerve through the lateral fillet and the auditory cortex. Moreover, the results of experimental investigations in degeneration accord with this view. After destruction of the auditory nerve nuclei, the secondary fibre system degenerates on the opposite side as far as the quadrigeminal bodies. Moreover, in general, the posterior quadrigeminal bodies are well developed in those animals alone in which there is a well-developed cochlea. Clinically, too, deafness has been caused (Gowers) by disease of these bodies.

It has been affirmed by many experimentalists and not a few clinicians that disease of the posterior quadrigeminal bodies produces disturbances of co-ordination and equilibration. It must be understood, however, that a diseased focus is rarely, if ever, limited to the corpora quadrigemina posteriora alone; neighborhood symptoms, as they are conveniently called, invariably occur. The disturbances of co-ordination resulting are doubtless due to some interruption in the underlying cerebellocerebral pathway, because the ataxia produced is distinctly cerebellar in type.

2. **The Anterior Quadrigeminal Bodies.**—(*a*) **The Fibrous Connections** of these bodies are with the lateral and mesial fillets, the superior brachium, and the nucleus of the motor oculi nerve.

(*a*) THE FILLET fibres pass into the stratum lemnisci of the anterior quadrigeminal bodies and apparently end there. That part of the mesial fillet which so terminates is usually known as the superior fillet. The physiologic explanation of these fibres is unknown.

(*β*) THE SUPERIOR BRACHIUM contains fibres coming to the anterior quadrigeminal bodies from two sources: (I) from the lateral root of the optic tract on its way from the retinal, and (II) from the occipital cortex, coming through the optic radiations of Gratiolet. The retinal fibres first spread out on the surface of the quadrigeminal bodies, forming the stratum zonale, and subsequently end by arborizing about the cells of the underlying layers. The occipital fibres end by arborizing about the cells of the stratum opticum.

(*γ*) THE FIBRES TO THE NUCLEUS OCULOMOTORIUS are the axones of cell bodies situated in the anterior corpora quadrigemina. They end by arborizing about the cells of the subnuclei of the third nucleus. Fig. 284 shows these anatomic connections.

The optic lobes or corpora bigemina of fishes, batrachians, and birds, are structurally homologous with the anterior corpora quadrigemina of mammals.

The facts of anatomy as well as those of physiologic and pathologic experiments indicate that the corpora quadrigemina, though not the centres of vision proper, are centres of co-ordination between retinal impressions and motor reactions or adjustments of considerable complexity. It is difficult, if at all possible, to differentiate clearly between the effects of lesions of the corpora quadrigemina and of those tracts with which they are related. In this connection a study of Fig. 285 may be suggestive. After extirpation of the eyeball in lower animals the stratum zonale atrophies, and in moles this layer is rudimentary. Evidently the anterior quadrigeminal bodies are chiefly concerned with ocular and pupillary movements. That such movements take place independently of the cerebral cortex is proved by the fact that when the hemispheres are removed the pupils will contract to light, and the eyes are moved in response to retinal impressions and in accordance with variations in the position of head and body.

(*b*) **Relation to Vision.**—That destruction of the optic lobes in lower animals undoubtedly causes blindness has long been known. Thus Flourens found that such destruction in birds caused blindness and dilatation of the pupils with cessation of their reactions to light; and he also found that the relations of the optic lobes were entirely crossed—*e. g.*, destruction of the left lobe causing total loss of vision in the right eye and destruction of the right lobe causing total loss of vision in the left eye. The crossed relations between the eyes and optic lobes have their foundation in the decussation of the optic tracts in the optic chiasms, but the extent of the decussation varies in different animals. For example, in cats and dogs experiments

FIG. 284

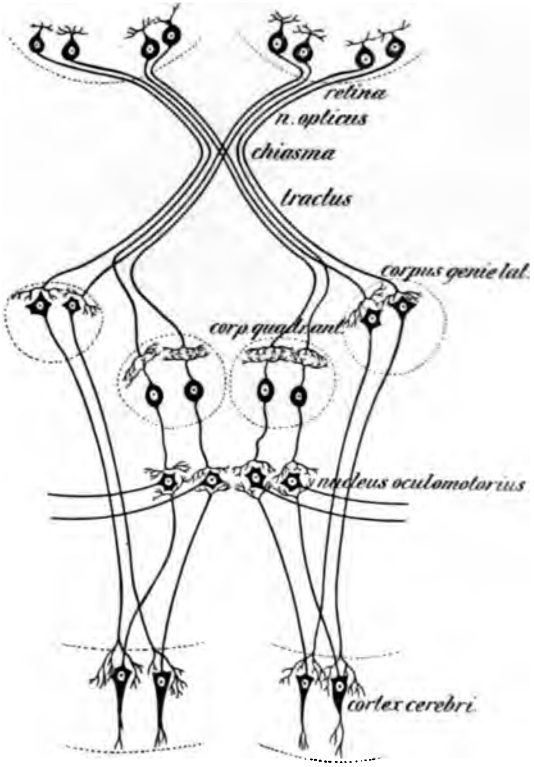
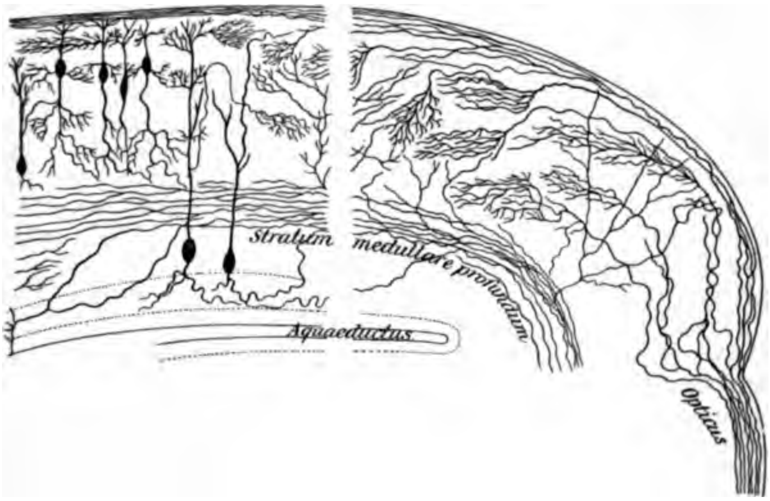


Diagram of the probable relations of some of the nerve cells and fibres belonging to the retinal and central visual apparatus. (Schäfer).

have shown that after enucleation of one eye partial atrophy occurs in both optic tracts, but to a much greater extent in the tract of the opposite side.

In man it is not probable that the anterior quadrigeminal bodies are directly concerned in the function of vision. Those clinical cases where such blindness occurs have been invariably due to tumors, and, as Gowers observes, were sufficiently explained by the optic neuritis present. In man stimulation of the anterior pair produces dilatation, first of the opposite pupil and then of the homolateral pupil. Indeed, the results of clinical study indicate that they are chiefly concerned, as already stated, in the adjustment of ocular movements to visual impressions; and such adjustment may be immediate through the optic tract; or mediate, impulses being sent backward from the occipital cortex to the anterior quadrigeminal bodies.

FIG. 285



Showing the minute structure of the midbrain roof. Two sections are placed side by side for comparison of the layers. The right-hand section is from a frog; the left-hand one from a lizard. Various connections may be traced between the optic tract and the stratum medullare profundum. When one remembers that the *tr. tectospinales et tectobulbares* are traced into the stratum medullare profundum we see a basis for Edinger's suggestion that "through this structure there arises an extraordinarily great opportunity for the transmission of light impressions to the general sensory tract." (Edinger, 5th edition, p. 116.)

(*c*) **Effects of Irritation.**—The excitability and effects of irritation of the anterior corpora quadrigemina or optic lobes, by various stimuli, have been differently stated by different observers. Ferrier maintains that mechanical irritation of the surface of these bodies is capable of inducing distinct indication of excitability. The act of merely touching these ganglia with a sponge is sufficient to cause general and more or less indefinite movements of the trunk and limbs. The slightest superficial puncture of the corpora quadrigemina in rabbits causes them to start suddenly and bound away as if in great agitation and alarm. These symptoms speedily subside and it is almost impossible to discover any signs of anatomic lesion from the slight puncture which is sufficient to give rise to these manifestations. Much, however, depends on the vital condition of these ganglia at the time of experiment. When they are exhausted by shock or hemorrhage or paralyzed by narcotics excitation may have little or no perceptible effects. The optic lobes have been found extremely sensitive to electric currents.

The explanation of the effects of irritation of the corpora quadrigemina and of the relation between these and the effects of destructive lesions is a matter of speculation only. Though electric stimulation is not strictly localizable, and there is always a risk of diffusion, it has been shown that mere mechanical irritation of the surface of the corpora quadrigemina is sufficient to produce motor manifestations, in which case obviously conduction to subjacent or neighboring tracts can play no part. The strength of current sufficient to produce active manifestations when applied to the surface of the corpora quadrigemina is very weak and barely perceptible when applied to the tip of the tongue; so that the risk of diffusion is very slight, and it is a fact which cannot be explained away by mere diffusion to subjacent structures. Irritation of the posterior quadrigeminal bodies differs from that of the anterior in at least one important particular, viz., the excitation of cries of various kinds. These are not observed on irritation of the anterior quadrigeminal bodies. If it were merely a matter of diffusion to subjacent tracts, the same results should occur in both cases.

3. **The Cerebellocerebral Pathway.**—Although there is still more or less disagreement among anatomists concerning this pathway, it is generally agreed that it consists of three or four neurones. The first apparently extends from the cerebral cortex, from either hemisphere or worm, to the nucleus dentatus. The second neurone extends from the nucleus dentatus, in which its cell body lies, forward through the superior cerebellar peduncle (brachium conjunctivum), decussates with its fellow, and enters the posterior and ventral portion of the red nucleus of the opposite side. The third neurone may extend directly from the red nucleus to cerebral cortex, or indirectly, by way of the optic thalamus or hypothalamic region. In the former case the cell body apparently lies in the dorsal and anterior portion of the red nucleus, while its axones extend up through the capsular region to the cerebral cortex. In the latter case the cell body sends its axone to the ventral portion of the optic thalamus or the hypothalamic region, where it ends by arborization. In such instances

a fourth neurone is required, extending from these terminations to the cerebral cortex. The portion of the cerebral cortex in this relation with the red nucleus and whole cerebellocerebral pathway is the region of the central gyri and operculum, possibly also the region of the island of Reil and the anterior part of the parietal lobe.

The function of this tract is undoubtedly the transmission of afferent impulses of some sort from the cerebellum. The cerebellar cortex, as we have seen, receives numerous fibres from the spinal cord through the corpus restiforme, the dorsal external arcuate fibres from the nuclei gracilis and cuneatus, and also a few spinal fibres from Gowers' tract *via* the superior cerebellar peduncle. Is it possible that the impulses so reaching the cerebellum may not be conducted to the cerebral cortex? The possibility certainly exists, but the fact is not as yet demonstrable. The main function of this pathway seems to be to put the cerebellar hemisphere of one side into close relation with the opposite cerebral hemisphere.

4. **The Nuclei of the Third and Fourth Cranial Nerves.**—The nucleus trochlearis supplies the superior oblique muscle. The nucleus lies immediately behind the oculomotor nucleus, and the axones of its cell bodies decussate in the superior medullary velum, then emerge on its dorsal surface, and proceed around the crustæ to their destination. The trochlear nucleus is intimately associated with the posterior longitudinal bundle, the function of which appears to be the co-ordination of the eye muscles, and of movements of eyes and head, or eyes and the muscles of expression. The oculomotor nucleus is far more complicated than the trochlear nucleus, consisting of no less than six paired nuclei and an unpaired one. These subnuclei in general send their axones in a curved direction downward through the tegmentum, red nucleus, and substantia nigra, to emerge at the posterior perforated space; but a set of fibres from the posterior third of the nucleus decussates to the opposite side. Each oculomotor nerve, therefore, contains fibres from the right and left oculomotor nuclei. By Spitzka and Obersteiner these decussating fibres are held to supply the opposite internal rectus muscle. Thus, a motor impulse from the cerebrum to the left oculomotor and abducent nucleus might lead to contraction of the left external rectus and of the right internal rectus muscle. According to Schwalbe, however, these crossed fibres pass to the superior rectus. According to Duval and Laborde the harmonious action of the external and internal recti muscles is secured by a set of fibres emerging from the abducent nucleus, proceeding cerebralward through the posterior longitudinal bundle, decussating and ending by arborizing about cells in the opposite oculomotor nucleus.

According to Hensen and Völckers the subnuclei of the oculomotor nuclei from before backward are arranged as follows: (I) nucleus of accommodation; (II) nucleus for the sphincter iridis; (III) nucleus for the internal rectus; (IV) nucleus for the superior rectus; (V) nucleus for the levator palpebræ superioris; (VI) nucleus for the inferior rectus; (VII) nucleus for the inferior oblique muscle. The disease known as polioencephalitis superior seems to afford excellent substantiation of these assertions clinically, the successive paralyses involving these subnuclei in this order of anatomic arrangement.

The oculomotor nucleus, besides numerous and important connections with the posterior longitudinal bundle, of very obvious advantage, is also directly connected with the optic radiations and the optic tract. It will be recalled that the superior quadrigeminal body was said to receive fibres from the optic tract, and also fibres from the cortex of the occipital lobe. These fibres are evidently of large importance in pupillary reactions.

5. **The Pes Pedunculi.**—This has but one function, that of conduction of impulses from the cerebral cortex. In the middle third lie the pyramidal tract fibres and the fibres to the nuclei of the seventh and twelfth cranial nerves. In the inner third lie the fibres of the frontal cerebrocorticopontine-cerebellar pathway. The axones from the pyramidal cells of the frontal cortex proceed toward the internal capsule, pass through its frontal portion, into the inner third of the pes pedunculi, and end at the cells of the nuclei pontis. The axones of these cells then decussate and proceed upward through the opposite middle cerebellar peduncle (brachium pontis) to the cerebellar cortex. Thus the cerebral hemisphere is brought into direct relationship with the opposite cerebellar hemisphere in a corticifugal way, precisely as it is by the cerebellocerebral pathway in a corticipetal way.

In the outer third of the crusta lie the fibres of the temporal cerebrocorticopontine-cerebellar pathway, the course and termination being in every way analogous to the frontal pathway. It is very likely that both of these great pathways, each occupying as much space in the pes pedunculi as is put at the disposal of the pyramidal tracts, are immediately concerned in carrying to the cerebellum impulses concerning co-ordination in its broadest sense. It would seem as though there went from the cerebral cortex, simultaneously with the general message through the pyramidal tract fibres, a set of impulses by way of the corticopontine-cerebellar pathway to the cerebellum, by means of which its co-ordinating power might be aroused.

b. Pathologic Physiology of the Mesencephalon.

Connected with the midbrain is what is known as *Weber's syndrome.* A more or less extensive lesion in the tegmentum of the midbrain, by reason of the fact that it cuts off the fibres of the third nerve on the side of the lesion and by reason of the fact that it involves the pyramidal tract fibres far above their decussation, causes what is called a crossed third paralysis. That is, for example, if the lesion were in the right half of the midbrain, the right oculomotor nerve and the left half of the body would be paralyzed. Since the mesial fillet would also be affected, sensory symptoms would be manifest on the same side of the body as the paralytic ones.

F. THE PHYSIOLOGY OF THE INTERBRAIN, OR THALAMENCEPHALON.

a. Normal Physiology.

Almost nothing is known of the physiology of the interbrain. Certain features of its structure are suggestive, however, of functions which it may some time be demonstrated to possess. In general it acts chiefly as a relay station, as a sensory centre, and as a centre of emotional expression.

1. **As a Relay Station.**—The optic thalamus, the main portion of the thalamencephalon, is essentially a receiving station. To it there come from the cerebral cortex fibres from the frontal and temporal regions, constituting a portion of the corona radiata; and from it large numbers of fibres pass to the cerebral cortex, chiefly to the occipital, temporal, and parietal lobes, constituting a still larger portion of the corona radiata. On the other hand, it receives from lower levels the fibres of the cerebellocerebral pathway by way of the red nucleus, fibres from the mesial fillet, and numerous less important bundles. The impulses conducted by these fibres ultimately reach the cortex, the optic thalamus being interposed as a relay centre; thus an intimate relationship between cerebral cortex and optic thalamus is manifest. That the development of the thalamencephalon is largely dependent upon that of the cerebrum is evident from the fact that "with the development of an extended cerebral cortex more and more bundles appear which pass from it into the ganglia of the thalamus,[1] or from the ganglia of the thalamus into it. In proportion to its enormous mass, the optic thalamus sends only a few fibres downward."

2. **As a Sensory Centre** the interbrain must be given some credit. Fig. 281 shows the lateral geniculate body, a part of the thalamus, as a way-station between the retina and the cerebral cortex of the visual centre in the occipital lobe. In a similar way the internal geniculate body is a way-station on the path of auditory sensation. Very likely, too, the interbrain is a motor centre for instinctive or emotional expression.

3. **As a Centre of Instinctive or Emotional Expression.**—Animals deprived of their cerebral hemispheres are still capable of exhibiting, in response to various forms of sensory stimulation,

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[1] Edinger, fifth edition, p. 134.

special and general reactions, more or less complex, which do not at all differ in character from those which are associated with emotion or feeling.

The outward expression of feeling does not necessarily imply the existence of pain or feeling as a state of consciousness. As all the physical manifestations of feeling are capable of being called forth in animals deprived of their cerebral hemispheres, which alone are the substrata of consciousness, we must regard them as merely the reflex or instinctive response of centres in which sensory impressions excite variously the motor, vasomotor, and secretory apparatus. The phenomena observed in animals deprived of their cerebral hemispheres are in all respects analogous to those observed in human beings under the influence of chloroform which, as proved by actual experiment, first annihilates the excitability of the hemispheres, a condition coinciding with abolition of consciousness—but the thalamencephalic and lower centres retain their excitability long after this point has been reached. Hence with impressions which under normal conditions would excite not only pain, but also accompanying groans, cries, or other physical manifestations, when the cerebral hemispheres have been removed the physical manifestations alone occur, and conscious suffering is absent.

The centres of emotional expression are, therefore, situated below the centres of conscious activity and ideation, and must necessarily be in relation with every form of centripetal and centrifugal impulses through which signs of feeling may be induced or manifested. These conditions are not furnished below the mesencephalic centres, and are best met in the thalamencephalon. Both direct experiment and clinical experience favor the latter as the emotional centre.

b. Pathologic Physiology of the Thalamencephalon.

Disease of the optic thalamus, alone and uncomplicated, is very rare. Slight hemiplegia, occasionally seen, is undoubtedly a neighborhood symptom due to involvement of the pyramidal fibres in the internal capsule. No disturbance of cutaneous sensation results, unless the posterior limb of the internal capsule be injured, in which case there may be hemianæsthesia.

Hemianopsia has been described in lesions of the pulvinar, without involvement of the optic fibres in the posterior limb of the internal capsule. Disturbance of facial expression has been observed in thalamic disease, with forced laughing and crying. Posthemiplegic hemichorea and hemiathetosis are ascribed to disease of the optic thalamus. Vasomotor symptoms do not seem to result, but the tendinous and periosteal reflexes are increased. In bilateral lesions of the optic thalami vesical incontinence follows, the urine being voided automatically at stated intervals in definite amounts.[1]

[1] Homburger, Neurolog. Centralblatt, 1903.

G. THE PHYSIOLOGY OF THE CEREBRUM, OR PROSENCEPHALON.

1. THE MOVEMENTS OF THE BRAIN.

Movements of the brain depend largely upon the lymphatic system of the encephalon. Our knowledge of this difficult subject may be attributed chiefly to the labors of Obersteiner, Key, Retzius, Schwalbe, Meynert, and Bevan Lewis. Obersteiner was the first to define the nature and connections of the lymph channels. Bevan Lewis is, however, to be credited with having given us the latest and most advanced details as to the relationship of the cortical nerve cells to these lymph channels, both in health and disease. It will perhaps simplify the subject if we diverge for a moment to consider the movements of the endocranial fluids, both blood and lymph, in general.

If the brain were surrounded merely by rigid cranial walls, and could never expand or contract, there would be possible no increase or decrease, with functional activity or rest, of the arterial blood within it. A functional increase becomes possible, however, upon one of two conditions, viz., a transfer of venous blood from the brain, or an outflow of lymph from the brain. A venous transfer is altogether too slow, and there could not be continuous action because the propulsion of the venous current, dependent upon the respiratory movements, would give rise to a frequently interrupted flow of venous blood from the brain. The lymph flow is not open to the same objections. The lymph within the brain is largely collected both in the ventricles and the so-called lymph cisterns, of which Meynert enumerates the following: (I) the space of the fossa Sylvii; (II) farther back, the cysterna chiasmatis; (III) another is to be found adjacent to the fossa, between the overhanging cerebellum and the pons and medulla. Much lymph, too, is accommodated in the perivascular spaces about all of the vessels of the brain cortex. All of these collections of lymph communicate very freely with the spinal canal; for by means of lumbar puncture, for example, one may drain the serum from a hydrocephalic head. Despite the fact that the brain is enclosed by rigid walls, it can, nevertheless, accommodate widely varying amounts of arterial blood, by reason of the freedom of outflow of the cerebrospinal fluid.

1. **Quantitative Relation between Blood and Cerebrospinal Fluid.**—There is, then, an intimate relation between the amount of cerebrospinal fluid and blood within the cranial cavity. Formerly it was taught that as the skull is a rigid box, and as the brain substance and its fluid are practically incompressible, no variation in the amount of blood in the brain could be possible. This, however, is now proved to be erroneous. The average quantity of cerebrospinal fluid within the

cranium is about two ounces, and if it be suddenly withdrawn epilepsy or convulsions may be produced, or if it be rapidly increased in amount coma may result. This fluid has also important mechanical functions, protecting delicate parts of the brain from injury, and distributing vibratory impulses. The presence of the cerebrospinal fluid is, as pointed out by Donders, of great importance in regulating the pressure uniformly when brain movements occur, so that every systolic and expiratory dilatation of the bloodvessels is concentrated upon those parts of the cerebral membrane which do not offer any resistance. We are now ready to consider the physiologic movements of the brain.

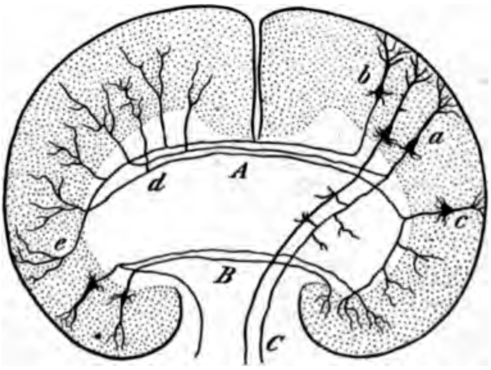
2. **Movements of the Brain.**—These are of three kinds: (I) Pulsatile movements communicated from the pulsations of the large basal cerebral vessels. (II) Respiratory movements; brain rising during expiration, and falling during inspiration. (III) Vascular elevation and depression, which alternate and are due to periodic dilatation and contraction of the bloodvessels. This last is a periodic arterial dilatation regulated by the vasomotor centres and occurring from one to six times per minute. These movements have been investigated chiefly over the fontanelles of children and where the membranes have been exposed by trephining. The advance of the dilatation wave within the rigid cranial walls aids in the establishment of currents of brain fluid whereby metabolic waste products are carried off through the lymphatic fluid. The brain and the fluid surrounding it are subjected to a certain mean pressure which depends upon the blood pressure within the vascular system. Naunyn and Schreiber showed that cerebral pressure must be slightly less than pressure within the carotid before the symptoms proper to pressure on the brain occur. The vascular wave causes an expansion of the cerebral mass, followed by a contraction.

Meynert concluded that all stimuli acting on the sensorium create vascular movements and disturb the periodic changes in the condition of the vessels; and that, of the psychic influences which may cause elevation of blood pressure, the emotions act more readily and bring about a greater change than purely intellectual processes. Great variations of brain pressure are almost constantly attended by symptoms of disturbances of the nutrition of the brain. If the pressure is moderate the symptoms may remain latent or only show themselves as headache, vertigo, weakness or disturbance of the sensory function. During sleep the circulation of the lymphatic fluid in the brain effects the removal of the waste products, and this is to a great extent dependent upon the vascular movements of the brain. Burckhardt regards the influence of this vascular wave as far more powerful than that of the respiratory wave. The irregularities of vascular wave movements which occur when the individual is awake indicate that in certain parts of the brain there is an independence of action, just as we know it to be the case in reflex arterial constrictions on the surface of the body.

Pulsatory movements originate from the circle of Willis; the arteries ascend and their currents are directed upward, as is also the case with the venous currents. The arteries at the base are first to enlarge with the blood flow, then the wave passes into all the branches of the vessels. The brain, however, is only able to enlarge concentrically toward the ventricles on account of the resistance offered by the roof of the skull to the swellings of the convolutions. This concentric swelling of the brain is almost constant and the pressure is neutralized in the ventricles, partly owing to the fact that there is a displacement of cerebrospinal fluid from them. When the engorgement of the walls of the ventricles ceases, the blood supply which reaches the cortex through the long arteries is carried downward.

The act of inspiration causes a fall; that of expiration causes an elevation of pulse wave. This influence is most noticeable during forced efforts of expiration and depends upon variations in the venous pressure. As a result of venous pressure, concentric swelling of the hemispheres occurs. The venous pressure acts from the vertex downward instead of from the base upward as does the pulse wave.

FIG. 286



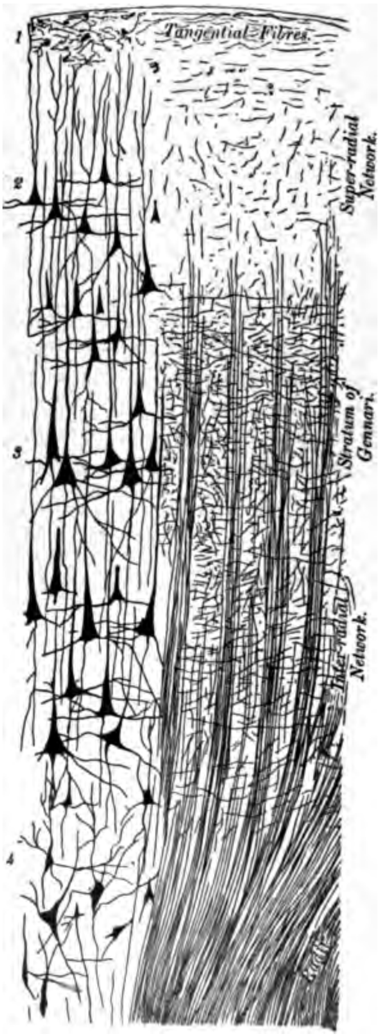
Transverse section of the cerebrum, showing the probable disposition of the commissural and projection fibres: *A*, corpus callosum; *B*, anterior commissure; *C*, pyramidal pathway formed of the projection fibres. (Cajal.)

2. THE FUNCTION OF THE CORTEX.

a. General Considerations.

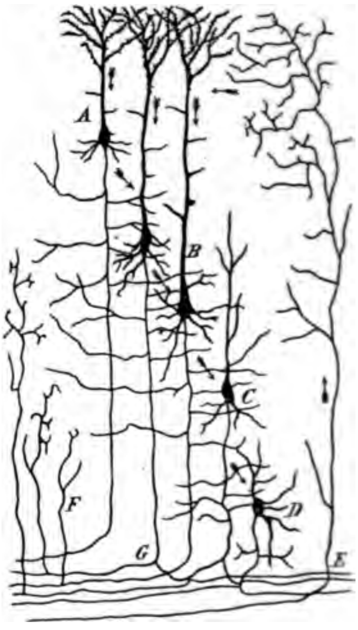
From numerous experiments of removal of the cerebral cortex in lower animals, one fundamental fact seems irrevocably established, viz.: *That in the absence of cerebral hemispheres, the lower centres* *are of themselves incapable of originating active manifestations of any kind.* When the hemispheres are removed all the actions of the animal become the immediate and necessary response to the form and intensity of the stimulus communicated to its afferent nerves. Without such excitation from the exterior the animal remains motionless and inert. It is true that some of the phenomena would seem opposed to this view, but this is only in appearance, not in reality. Thus a frog may occasionally move its limbs spontaneously and a bird may yawn, shake its feathers, or change the foot, but these actions are the result of impressions arising from

FIG. 287



Human cortex stained with Weigert's hæmatoxylin on the left, and by Golgi's method on the right.

FIG. 288



Probable direction of the currents and the nervous protoplasmic connections in the cell of the cerebral cortex: *A*, small pyramidal cell; *B*, large pyramidal cell; *C*, *D*, polymorphous cells; *E*, terminal fibre coming from other nerve centres; *F*, collaterals of the white matter; *G*, axis-cylinder bifurcating in the white matter. (Cajal.)

cutaneous irritation caused by the wounded surface resulting from the operation. The reader will find it profitable at this point to make a careful study of Figs. 286, 287, and 288.

If we enquire into the nature of the processes which immediately precede this responsive activity, we are led to ask, Are these actions merely reflex or are they accompanied by sensation? If we define sensation as the consciousness of impression, it will be seen that the problem which confronts us for solution is whether there is a consciousness accompanying the acts of these animals that are minus their cerebral hemispheres; in other words, are these animals, under the conditions of the experiments, capable of psychic activity?

If we were to accept without question the metaphysical view, the answer would not be difficult, viz., that abolition of the hemispheres abolishes certain fundamental powers of mind, that the functions of the lower centres lie outside of the sphere of the mind proper. But this way of looking at the subject does not harmonize with known physiologic facts. It is known that areas may be cut away from the hemispheres involving the territory of intellectual consciousness without interfering with consciousness; the will may be abolished while consciousness remains. Hence, we are not entitled to say that mind as a unit has a local habitation in any one part of the cerebral hemispheres, but rather that *mental manifestations depend on the conjoint action of all of the cerebral cortex.*

b. Localization of Functions in the Cerebral Cortex.

The following words of Herbert Spencer,[1] though written years ago, deserve to be quoted: "Whoever calmly considers the question cannot long resist the conviction that different parts of the cerebrum must in some way or other subserve different kinds of mental action. . . . . Localization of function is the law of all organization whatsoever, and it would be marvelous were there here an exception. Either there is some arrangement, some organization in the cerebrum, or there is none. If there is no organization the cerebrum is a chaotic mass of fibres incapable of performing any orderly action. If there is some organization it must consist in the same physiologic division of labor in which all organization consists, and there is no division of labor, physiologic or other, but what involves the concentration of special kinds of activity in special places."

Up to a comparatively recent date, the results of experimental physiology and human pathology had been considered as opposed to the localization of special functions in distinct regions of cerebral hemispheres. Many unquestionable facts of clinical medicine, however, such as limited paralysis in connection with limited cerebral lesions, appeared wholly inexplicable except on the hypothesis of a differentiation of function in the cerebral hemispheres. Moreover, the established coincidence of aphasia or loss of speech, with disease of a certain region in the left hemisphere, served still further to cause thoughtful students of this subject to seek rational explanations upon the basis of a differentiation of function in the cerebrum.

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[1] Principles of Psychology, 1870.

Hughlings Jackson, from a minute and careful study of the phenomena of unilateral and limited epileptiform convulsions, arrived at the conclusion that they were due to irritation or discharge of energy from certain convolutions of the opposite cerebral hemisphere, functionally related to the corpus striatum and muscular movements. Though he furnished many arguments in favor of this hypothesis, since verified, his views were regarded, at the time, as merely ingenious speculations and devoid of any actual proof that the gray matter of the convolution was really excitable. Experimental physiologists had all failed to obtain evidence of the susceptibility of the cerebral cortex to any of the ordinary stimuli of nerves, mechanical, chemical, thermal, or even electric. This apparent inexcitability of the cerebral cortex greatly retarded the progress of cerebral physiology.

A new era in cerebral physiology was inaugurated by the discovery by Fritsch and Hitzig in 1870 that the application of the galvanic current to the surface of the cerebral hemisphere in dogs gave rise to movements on the opposite side of the body—movements which varied with the position of the electrodes.

The phenomena of localized and universal convulsive movements, attributed by Hughlings Jackson to vital irritation of certain regions of the cortex, are precisely of the same nature as those induced by electric irritation of the same region. The great and significant feature of the reactions produced by electric excitation of the cortex is that they are definite, may be predicted, and vary with the position of the electrodes. So, as will be seen later, areas in close proximity to each other, separated only by a few millimetres or less, react to the electric current in a totally different manner. If there were no functional differentiation of the areas under stimulation the diverse effects would be absolutely incomprehensible on any theory of mere physical conduction.

1. **Localization of Motor Centres.**—At the outset it is important to emphasize the fact that the so-called motor cortex is not a centre for individual muscles, but is a centre for *movement complexes*. In the spinal cord, which is the lowest motor centre, the anterior-horn cells actually control individual muscles and muscle fibres; so that a lesion of these cells paralyzes a particular muscle or part of it. The effect of such paralysis is interference with all motor acts in which that muscle plays a part. In the cerebral cortex, however, individual muscles are not represented; instead there are to be found centres for various movements or acts, which commonly bring into

play several muscles, controlled at various spinal levels simultaneously by the cortical pyramidal tract fibres. The effect of injury to a particular portion of cortex is, then, the loss of ability to execute some particular movement or act, and not the paralysis of any particular muscle.

Another important clinical observation confirmed by direct experiment is that the *various motor centres of the cortex overlap one another.* There is, then, no sharp line of demarcation between the centres for extension of the fingers and flexion of the fingers. Our knowledge of this important fact and our knowledge concerning the location of our movement centres have been derived from three chief sources: (I) experiments upon the cortex of the brain of monkeys; (II) electric stimulation of the cortex of the brain of human beings during the progress of a brain operation, such stimulation being applied for the purpose of localizing the diseased area; (III) clinical evidence afforded by Jacksonian epilepsy and cerebral tumors, with subsequent post-mortem examination.

(*a*) **Experiments upon Monkeys.**—The surface of the cerebral hemispheres in monkeys is divided into certain lobes and convolutions by primary and secondary fissures. The general arrangement of these varies somewhat from that of the human brain; however, the homologies may be traced with fair accuracy, and the results obtained from experiments are indicative of the functions of homologous areas of the human brain. Electric stimulation of certain areas gives rise to definite response. The following are the principal phenomena usually observed:

(I) *Stimulation of the upper portion of the ascending parietal lobule* causes the opposite hind limb to be advanced as in walking, the thigh being flexed on the pelvis, the leg extended, the foot flexed, and the toes spread and extended. (See Fig. 289.)

(II) *Of the upper extremity of the ascending parietal and adjoining portion of the ascending frontal convolution:* Flexion, with outward rotation of the thigh; rotation inward of the leg with flexion of the toes.

(III) *Of the ascending frontal convolution, at the base of the superior frontal:* Extension forward of the opposite arm as if the animal tried to reach and touch something in front.

(IV) *Of the ascending frontal convolution at the bend of the knee of the præcentral sulcus:* Flexion and supination of the forearm.

(V) *Of the ascending frontal convolution below:* Retraction and elevation of the angle of the mouth.

(VI) *Of the ascending frontal convolution below:* Elevation of the ala of nose and upper lip.

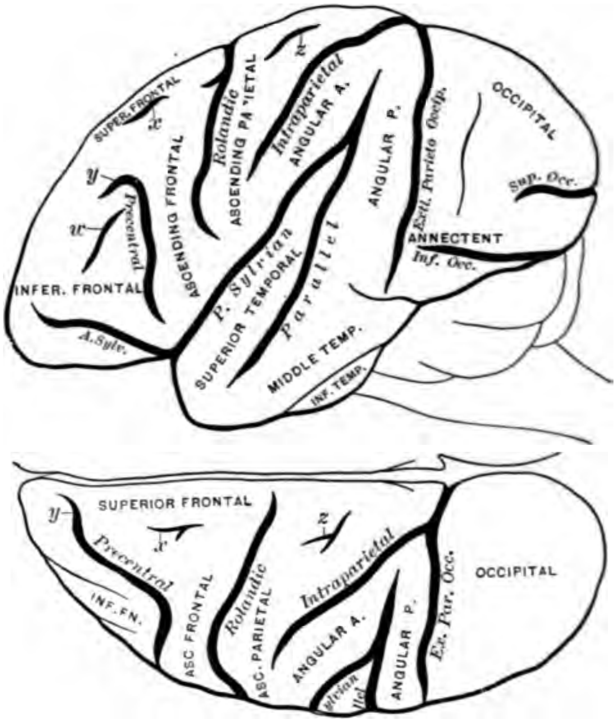
(VII) *Of the lower extremity of the ascending parietal convolution:* Opening of the mouth with protrusion and retraction of the tongue.

(VIII) *Of the lower extremity of the ascending parietal convolution:* Retraction of the angle of the mouth.

(IX) *Of the superior temporal convolution:* Pricking up of the opposite ear, turning of the head and eyes to the opposite side, and dilatation of the pupils.

(X) *Stimulation of the central lobe,* or Island of Reil, causes no motor reactions.

FIG. 289



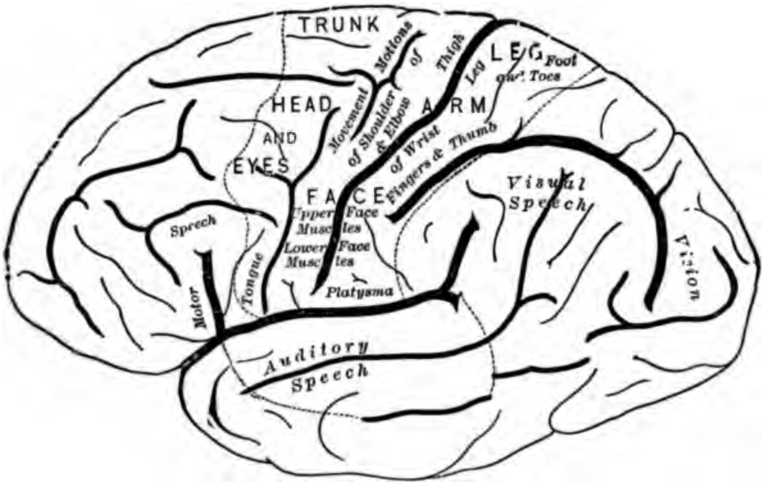
Outline of brain of monkey (*Macacus*) to show principal sulci (fissures) and gyri (convolutions). Natural size. Over each sulcus, purposely printed very thick, the name is written in *italics*, over each gyrus in SMALL CAPITALS. *x* indicates the small depression, hardly to be called a sulcus, which is supposed to be homologous with the superior frontal sulcus of man, and *w*, *y*, *z*, similarly indicate sulci whose homologies are not certain. (Foster, after Horsley and Schäfer.)

(XI) *Stimulation of the occipital lobe* causes no motor reaction.

(XII) Horsley and Beevor have made important contributions to the physiology of the mesial aspect of the brain. They found that *the marginal convolution*—located above the callosomarginal fissure—is excitable throughout, except in the prefrontal region.

(*b*) **Observations upon the Human Brain.**—These strongly confirm the above experimental results, and have been already sufficiently numerous to outline with considerable accuracy the various subdivisions of the motor cortex. The motor area of the human cerebral cortex is located, like that of the monkey, upon either side of the fissure of Rolando on the lateral aspect of the cerebrum, and upon the posterior portion of the marginal convolution on the mesial aspect of the cerebrum. The convolutions are, therefore, the ascending frontal, the posterior extremity of the first, second, and third frontal convolutions, the ascending parietal, and the posterior portion of the gyrus marginalis. In addition a motor centre used in governing the movements of the head associated with listening is to be found in the cortex of the temporal lobe. For obvious reasons the determination of the minute fields in the motor area which serve as centres for very limited movements has not advanced as far in the human subject as in the monkey. On the other hand, and for reasons just as obvious, the determination of the location and outline of the speech

Fig. 290



Functional areas of the cerebral cortex on the left side. (Dercum.)

area has progressed much farther in man than the monkey. (See Figs. 290 and 291.) The chief motor areas follow:

(I) *Larynx.* Annectant gyrus between the base of the ascending frontal and the ascending parietal gyri.

(II) *Tongue.* Base of the ascending frontal gyrus, overlapping to quite an extent the contiguous portion of the ascending parietal gyrus.

(III) *Face.* Contiguous portions of ascending frontal and parietal gyri, behind the inferior frontal gyrus.

(IV) *Thumb.* Contiguous portions of ascending frontal and parietal gyri, just above (III).

(V) *Fingers and Wrist.* Contiguous portions of ascending frontal and parietal gyri, posterior to the pars inferior of the middle frontal gyrus.

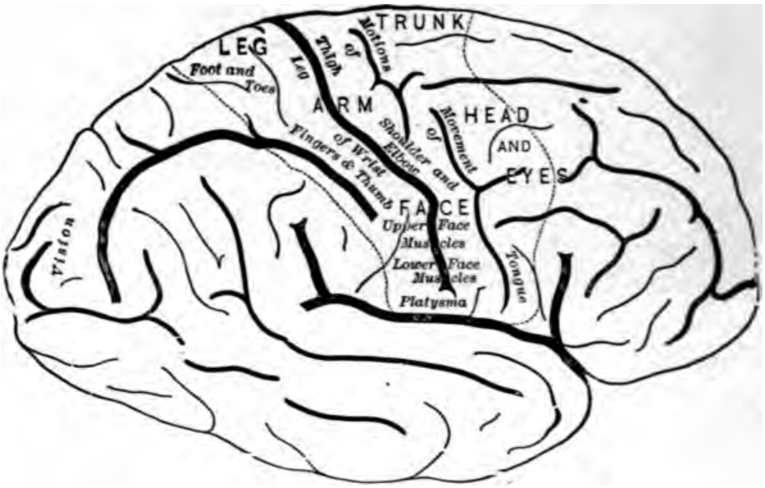
(VI) *Exner's Writing Centre.* Posterior portion of the middle frontal gyrus, and the contiguous portion of the ascending frontal gyrus; on the left side of the cerebrum, in right-handed people. Possibly this centre does not exist as a separate entity, but is merely the centre for the highly specialized finger movements necessary in writing, and is, therefore, present only in the left side of the brain in the right-handed, since only the right hand is trained in writing.

(VII) *Forearm.* Ascending frontal and parietal gyri, posterior to the pars inferior of the middle frontal gyrus.

(VIII) *Arm.* Immediately above (VII).

(IX) *Movements of Mastication.* Posterior portion of the pars superior of the middle frontal gyrus.

FIG. 291



Functional areas of the cerebral cortex on the right side. (Dercum.)

(X) *Trunk.* Posterior end of the first or superior frontal gyrus, and the adjacent portion of the ascending frontal.

(XI) *Thigh.* Upper ends of the ascending frontal and parietal gyri.

(XII) *Calf and Leg.* Ascending frontal and parietal gyri, posterior to (X).

(XIII) *Foot and Toes.* Ascending parietal gyrus and posterior portion of the gyrus marginalis.

(XIV) *Movements of Head in Listening.* Middle portion of first temporal gyrus.

(XV) *Associated Movements of Eyes and Head, as in Looking.* Posterior portion of the pars inferior of the superior frontal, and of the pars superior of the middle frontal gyrus.

(XVI) *Movements of the Eyeballs Alone.* Gyrus angularis.

(*c*) **Motor Speech Centre.**—This centre is of such transcendent importance as to demand special consideration. It is located in the posterior half of the third or inferior frontal gyrus, on the left side of the brain, in right-handed people. It is therefore a unilateral, instead of a bilateral centre. Since Broca (1861) was the discoverer of the location of the motor speech gyrus, it is often called Broca's convolution. Lesions of this left gyrus produce what is called motor aphasia, the patient being unable to utter words.

(*d*) **Higher Motor Centres.**—It is not likely that we originate motion in the so-called motor areas of the cortex. Probably there are three motor levels: (I) the highest cortical centre, (II) the motor area in the ascending frontal and ascending parietal gyri, and (III) the ventral cells of the spinal cord. The highest centre is probably in the frontal lobe. A case of Dieulafoy,[1] with a lesion in the anterior part of the left frontal lobe, suffered from Jacksonian epilepsy; and Dieulafoy has collected five other cases of motor disturbances involving the frontal cortex. It appears that the idea of motion may originate in some higher centre, that the proper impulses are then sent to the motor cortex, that this in turn incites the ventral cells in the spinal cord, and that these cells cause the proper muscles to contract. In favor of the idea that these highest motor centres exist, and that they are in relation to the motor areas on either side of the fissure of Rolando, is the additional fact that what is known as transcortical disturbances of movement occur clinically. This indicates the existence of a path of association fibres uniting a highest motor centre with the intermediate centre in the so-called motor cortex.

2. **Localization of Sensory Centres.**—These are the somæsthetic centre, the visual centre, the auditory centre, the olfactory centre, and the gustatory centre.

(*a*) **The Somæsthetic Centre** is the area of the cortex devoted to the reception of impulses of general sensation, tactile, thermal, algesic, and muscular, and is very extensive, standing in relation with the extent of the body surface. It is made up of the ascending frontal and parietal gyri, of the posterior ends of the superior, middle, and frontal gyri, of the posterior two-thirds of the gyrus marginalis, and of the adjacent portion of the gyrus fornicatus. As yet knowledge is too imperfect to permit of stating definitely just what portions of the surface of the body are in relation with the various portions of the somæsthetic area, but in a general way it may be affirmed that the portions of the body controlled by the motor cortex deliver their somæsthetic impulses to the corresponding motor areas. Horsley believes that the cells receiving tactile impulses are those located in the granular layer of the so-called motor cortex; and that the cells receiving muscular impulses are those located in the layer of small pyramidal cells. There are doubtless several levels for sensory impulses, the optic thalamus being one of the lower ones. From this level impulses pass to the somæsthetic area, where they are probably perceived in an elementary way.

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[1] La semaine méd., October 23, 1901.

Stereognosis.—A highest sensory centre, however, undoubtedly exists, and in the so-called stereognostic sense has its exemplification. An individual, grasping an object, as, for example, a pocket knife, can tell what it is without looking at it, merely from its "feel." This latter depends upon several qualities: the sense by which its weight is judged of, the tactile sense, the thermal sense, the space sense. If any one of these senses is gone, the ability to identify an object by "active touch" is impaired or lost; yet, on the other hand, cases have occurred where each one of these senses has been preserved, and still the stereognostic sense has been lost. Clinically, the sense is localized in the superior parietal convolution, a so-called silent area. But, as Flechsig has shown, this area is rich in association fibres, though very poor in projection fibres. It is evidently then an associational area. To it are doubtless transmitted all the various elementary impulses, from the correlation of which the identification of an object follows. The highest somæsthetic memory centres are probably located in the superior parietal convolution.

(*b*) **The Visual Centre.**—As in general sensation, so in vision, there are several levels. The retina itself is the first level of vision; the pulvinar constitutes a second level, and the lower cortical level lies in the cuneus of the occipital lobe, chiefly involving that portion next the calcarine fissure. The relation of this area to the eye is partially crossed—*i. e.*, visual impulses from the left eye reach the left cuneate gyrus from the temporal half of the retina, and the right cuneate gyrus from the nasal half of the retina. Injuries of the cuneate gyrus will, therefore, result in hemianopia, in which half of each retina is blended. If, for example, the left cuneate gyrus is destroyed, the left half of each retina is rendered blind and the right half of each visual field is therefore lost, since rays of light from the right field are the ones which fall upon the left half of the retina. Injury to the optic radiations of Gratiolet produces the same results, since they interrupt the course of the impulses to the visual cortex.

There are, however, higher visual centres. One may have the mere sensation of seeing something, but if there be no memory of the thing having been previously seen, there is and can be no recognition of the object. There must be, then, a higher visual centre for the storage of visual memories. This is believed to be in the gyrus supramarginalis, and to be bilaterally represented. Especially interesting is the centre for the location of visual word memories; this centre being located either in the gyrus supramarginalis or angularis or both, in the left cerebral cortex, in right-handed people. This centre is therefore a unilateral one.

(*c*) **The Auditory Centre.**—Impulses of hearing have been already traced by way of the lateral fillet to the auditory cortex, which lies in the first and second temporal gyri. It is certain that each ear is connected with the cortex of both sides of the brain; hence cortical lesions of the temporal gyri do not produce deafness. Just as in the case of vision, we must postulate a higher memory sound centre. We may hear the call of a particular bird as a mere sound, or we may hear the call and at the same time recollect what sort of bird made the call before, and on what occasion we heard it. There are, then, two auditory levels—a level for the perception of mere sound, and an identification level. So far as is now known these two levels are bilateral. A third level, a centre for the identification of spoken words, the so-called verbal auditory or word centre, lies in the middle portion of the left first temporal gyrus in right-handed people.

(*d*) **The Olfactory Centre.**—The olfactory tract in man is anatomically very imperfectly understood. The olfactory apparatus really originates as a distinct morphologic entity, the rhinencephalon. Indeed, in many of the lower mammals only rudiments of the pallium are possessed, most of the cerebral hemispheres consisting of the rhinencephalon alone, the olfactory lobe really constituting one-half of the entire forebrain. In man, on the other hand, the rhinencephalon is poorly developed, and the pallium develops as in no other animal. Impulses pass from the olfactory membrane to the olfactory bulb, thence backward through the olfactory tract. The fibres of the mesial root extend along the inner side of the brain to the septum pellucidum, over this into the fornix, and thence to the cortex of the cornu Ammonis. The fibres of the lateral root pass backward over the anterior perforated space and disappear in the uncus of the hippocampal gyrus. Intimately connected with the olfactory apparatus are the fornix, the striæ pineales, the ganglion habenulæ, the fasciculus retroflexus, and the bundle of Vicq d'Azyr. The hippocampal gyrus seems to be the centre for the reception of olfactory impulses, and the fornix appears to connect the cornu Ammonis with the optic thalamus. The centre for the memory of smells and odors, by which identification is made possible, may lie in or near the uncus of the hippocampal gyrus.

(*e*) **The Gustatory Centre** is even more hazy than the olfactory. A lower and higher centre undoubtedly exist, the lower for the mere perception of taste, the higher for the memory of tastes. The taste centre is said to lie in the fourth temporal gyrus.

3. PATHOLOGIC PHYSIOLOGY OF THE CEREBRAL CORTEX.

Aphasia. (*a*) **General Considerations.**—Words are related to the cerebral cortex in four ways: they can be spoken and written, and they can be read and heard. We have, therefore, four chief varieties of word losses dependent upon cortical injury: (I) inability to speak, called motor speech aphasia, or aphemia; (II) inability to write, called graphic motor aphasia, or agraphia; (III) inability to read, called visual aphasia, or word blindness; (IV) inability to understand spoken words, called auditory aphasia, or word deafness. As has already been stated, the cortical seat for motor speech is the left third or inferior frontal convolution; the seat of written speech is Exner's writing centre, or the posterior portion of the left middle frontal convolution; the seat for the reading of written words is the left gyrus angularis; and the seat for hearing words is the middle portion of the left first temporal convolution.

Attention is called to the accompanying Fig. 292, which shows how the primary word centres are mutually dependent. Thus writing from dictation presupposes a path from *D* to *A*, for the words are first heard, and are then committed to paper. In any school-room the importance of educating this pathway is fully appreciated. Reading aloud is also necessarily taught. The words are read at *C*, and an associational or transcortical path leads to *B*, whereby the words are spoken. Copying from a copy-book is a proper educational measure, for the words are read and appreciated at *C* and put on paper by the centre A. The earliest transcortical path cultivated is from *D* to *B*. The infant hears the words at *D*, and says them after the person speaking them through the centre *B*.

FIG. 292

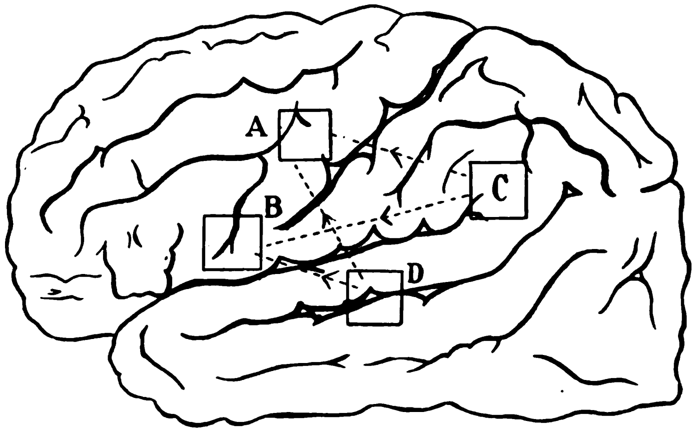

Diagram to illustrate aphasia: *A*, writing centre; *B*, motor speech centre; *C*, visual word centre; *D*, auditory word centre.

Individuals vary greatly, as was originally pointed out by Charcot, in the receptive capacity of the primary word centres. Most people retain tenaciously that which they hear; hence lectures are the favorite medium for advanced instruction. Others can learn only by committing things to paper; hence the method of learning by the formation of abstracts or synopses is common among students. In general it may be affirmed that nothing is well known unless it is lodged in two centres with a well-defined associational pathway between. Many students find the *D A* or the *C A* pathways the most efficacious; taking notes on lectures or abstracting text-books. Primary-school children, as a rule, begin with the *C B* and the *D B* pathways, learning to read aloud or learning by repeating "in concert" after a teacher. It is only the more advanced student who cultivates the *D A* and the *C A* pathways, involving the writing centre.

(*b*) **Classification** in general aphasia is said to be *simple* when it involves a primary word centre, as *A*, *B*, *C*, or *D*. It is said to be *combined* when it involves two centres, and these centres must be adjacent, the usual combinations being *A B*, *B D*, and *C D*. Owing to the wide separation of *A* and *C*, the *A C* combination scarcely exists. Aphasia is said to be *transcortical* when it involves an associational pathway, as the lines *D B*, *D A*, *C B*, and *C A*. Of these the one which is the best known is the D B pathway. An individual afflicted with such a lesion has what is called paraphasia. Speech is possible, because the motor speech centre *B* is intact, but since the connection between word hearing and motor speech is broken, the patient is unable to correct his own mistakes, of which he makes large numbers. For further information concerning this important subject the student is referred to the various text-books upon nervous diseases.

4. FUNCTION OF THE CORPUS CALLOSUM.

The great central commissure has long been a subject of much speculation as to its physiology. Putnam[1] has gathered together thirty-eight cases of tumor of the corpus callosum confirmed by post-mortem examination, and has arrived at valuable conclusions. The main defects are progressive failure of mentality, rapidly developing stupor, and absolute physical and mental inertia. The power of initiative seems to be wholly lost. Spitzka sees in the development of the corpus callosum an index of the mental development of the individual.

5. FUNCTION OF THE CORPUS STRIATUM.

Careful pathologic and clinical study goes to show that the lenticular nucleus has some control of motion, since lesions of this nucleus result frequently in dissociated paralyses, the adjacent internal capsule being uninjured.[2] Possibly this nucleus is a place for the passage or origin of a group of motor fibres destined for the opposite side of the body. Lesions of the right lenticular nucleus cause no speech disturbances. Lesions of the left nucleus cause such disturbances if they are located in the mesial portion, or at the ansa lenticularis. No sensory function is attributable to the corpus striatum. According to Hale-White and others, brief increases of temperature result from both experimental injury and spontaneous disease of this body. It is therefore supposed to contain one of the heat-regulating centres.

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[1] Journal of Nervous and Mental Diseases, 1901.

[2] Mingazzini, Rivista sper. de Fren e Meg. leg., xxvii. and xxviii.

6. FUNCTION OF THE INTERNAL CAPSULE.

The function of the internal capsule is purely conductive. Since it is the first point where all the motor pathways from brain to cord, and all of the sensory pathways from cord to brain, meet and pass one another, its importance from a clinical standpoint is immense. The function of those fibres, which lie in the anterior limb, is unknown. Since disease of the angle and the anterior half of the posterior limb causes contralateral hemiplegia, involving both face and tongue, as well as speech, we know that this area represents the motor portion of the capsule. The remaining portion of the posterior limb is engaged in conducting to the cerebrum impulses of general sensibility from the opposite side of the body, as well as impulses of taste, smell, hearing, and sight. Vasomotor fibres are also evidently located in the posterior limb of the internal capsule.

7. HIGHER CEREBRAL FUNCTIONS.

It is not within the province of this brief manual to discuss higher cerebral functions or the intellect of man. For a treatment of this subject the student is referred to the various works on psychology.

Innumerable clinical observations make it certain that the physical basis of the mind of man is the cerebral cortex. That certain attributes of the mind are lost with the functional destruction of certain portions of the cortex indicates that the localization of function is not confined to sensation and to volition.

Through the interrelation and interaction of cerebral centres one is not only conscious of sensation, but he interprets the sensation, referring it to some object outside of the brain itself. Such an interpretation of sensation is called *Perception*.

Sensations and perceptions affect the brain structure in some mysterious way leading to a retention of the impression, with ability on the part of the subject to call up the impression again: *Memory* and *Recollection*.

Through the aid of the memory a series of sensations and perceptions may be combined into a clear mental picture: *Conception*.

Conception merges into *Imagination*, for the latter is the "power of the mind to create mental pictures out of the data derived from experience." These mental pictures may either be faithful reproductions of previous sensations and perceptions: *Representative imagination* (Conception); or the mind may construct entirely new pictures combined from various elemental sensations and perceptions: *Constructive imagination*, or *Imagination proper*.

Given the powers enumerated and defined above the mind is able to make a series of judgments or conclusions—*i. e.*, to *Reason*.

As a result of reason the subject may deliberately enter upon a certain line of action. The power of the mind *to will to do* is called *Volition*, or *The Will*.

Sensations through the medium of memory may call forth in the mind a series of *Emotions:* fear, anger, love, hatred, etc.

CHAPTER XII.

THE PHYSIOLOGY OF THE MUSCULAR SYSTEM.[1]

A. GENERAL ACTIVITIES OF MUSCULAR TISSUE.

B. ENUMERATION AND CLASSIFICATION OF THOSE MUSCULAR ACTIVITIES ARISING FROM A CHANGE IN FORM.

1. THE INVOLUNTARY MUSCLES.
2. THE VOLUNTARY MUSCLES.
   (*a*) MUSCULAR ORGANS: THE TONGUE.
   (*b*) MUSCLE-BONE ORGANS: THE SKELETAL MUSCLES.
      (1) *General Functions of Muscle-bone Organs.*
      (2) *Special Functions of Muscle-bone Organs.*
      (3) *Animal Mechanics.*

A. GENERAL ACTIVITIES OF MUSCULAR TISSUE.

UNDER the influence of the nervous system various chemical, thermal, electric, and morphotic changes occur in constant succession in muscle tissue. In our study of metabolism we found that in this tissue the most active metabolic changes take place. Even when a muscle is said to be resting, *i. e.*, not undergoing morphotic changes, the metabolism within the tissue may be very active.

(*a*) CHEMICAL CHANGES.—Under general metabolism we found that muscle tissue is the scene of important chemical changes. Most important among these changes is the oxidation of dextrose, with the attendant consumption of oxygen and liberation of CO_2 and H_2O. The katabolism of energy-producing ("circulating") proteins must now be recalled. The result of this katabolism is the formation of nitrogenous (kreatin, etc.) and non-nitrogenous molecules of simple structure ($CO_2 + H_2O$, etc.). Next in importance is the destructive metabolism of muscle protoplasm. Incident to this katabolism oxygen is consumed, and CO_2, H_2O, and a nitrogenous molecule—kreatin, for example—are liberated. Recent investigations in this field make it certain that a part at least of the carbon, hydrogen and oxygen liberated in muscle katabolism takes the form of sarcolactic acid—$CH_3{\cdot}CHOH{\cdot}COOH$—which gives the acid reaction to fatigued muscle.

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[1] Introductory to this subject review, under General Physiology, the topics: "Motion" and "Contractility."

(β) THERMAL CHANGES.—Incident to the katabolic changes just enumerated energy must be liberated. This energy may take different forms. In a resting muscle the energy is liberated in the form of heat. Recall the fact that the muscle tissue is the tissue of thermogenesis. It is probable that in simple thermogenesis the katabolism involves almost exclusively the dextrose and "circulating" or energy-producing proteins, leaving the muscle protoplasm unimpaired. The thermogenetic activity of muscle tissue is under the direct control of thermogenetic centres in the brain.

(γ) ELECTRIC CHANGES.—Katabolism of muscle tissue and of circulating nutrients within muscle tissue is always attended with the liberation of heat energy. It may or may not be attended with the liberation of electric energy. It seems fairly well established that electric changes manifest themselves only when the muscle contracts (the current of injury—demarcation current—excepted). That part of the muscle where the contraction wave begins is electronegative to that part of the muscle yet uninfluenced by the contraction wave. In the beating heart the base is electronegative to the apex when the systole begins, and at the end of systole the apex is electronegative to the base.

(δ) CHANGES OF FORM.—One of the forms of energy liberated in muscle metabolism is mechanical energy. Mechanical energy manifests itself by moving matter through space. In the locomotion of an animal mechanical energy is manifested. Animal locomotion in higher animals is performed by use of the skeletal structures as levers. The levers are set in motion by the tension of muscle tendons. This tension is possible only as a result of a *change* of *form* of the muscle. The muscle contracts by increasing its lateral dimensions at the expense of its longitudinal dimensions. This brings the origin and insertion of the muscle nearer together. If the origin of the muscle is a fixed point, tension will be exerted upon the insertion. Thus the change of form of muscles makes it possible for them to perform mechanical work as one of the manifestations of the energy liberated in muscle metabolism.

B. ENUMERATION AND CLASSIFICATION OF THOSE MUSCULAR ACTIVITIES ARISING FROM CHANGE IN FORM.

1. THE INVOLUNTARY MUSCLES.

1. Non-striated Involuntary Muscles. (*a*) CHARACTER OF CONTRACTION.—Slow, somewhat prolonged, and relatively weak. *Examples:* (I) Peristaltic contraction of walls of alimentary canal and of ducts of associated glands. (II) Contraction of bladder in act of micturition. (III) Contraction of walls of bloodvessels. (IV) Contraction of uterine walls in act of parturition. (V) Contraction of ciliary muscles in act of accommodation. (VI) Contraction of the *erector pili* muscles in "*Cutis anserina.*" (VII) Contraction of gland ducts in general.

(β) MECHANICS OF MOVEMENTS PRODUCED BY UNSTRIPED MUSCLE.—In examples (I), (II), (III), (IV), and (VII) the walls of the cylindric or subspheric organs in question contract upon the more or less fluid contents of the organs. There is no leverage and no antagonistic muscular action. The contraction produces pressure of the wall toward the centre of the enclosed space. The pressure is equal upon all equal areas of the wall, and the tendency is to drive the liquid contents toward the direction of least resistance, toward the physiologic outlet of the cavity. In examples (V) and (VI) the muscles contract against the elasticity of certain tissues which oppose their action. During relaxation of the muscle the elasticity of the tissues restores the relations of the tissues to their usual position.

2. **Striated Involuntary Muscle.** THE HEART IS A STRIATED INVOLUNTARY MUSCLE.—The *contractions of the heart are peristaltic in character.* Though peristalsis is somewhat obscured in the heart action in higher vertebrates, one has only to refer to the action of that organ in lower vertebrates or in the embryonic life of higher vertebrates to be convinced of the truth of the statement. The character of the contractions of heart muscle differs very much from that of other involuntary muscles: first, in the rapidity of the contractions; and second, in the force of the contraction. It is probable that the striation is the effect of this difference of action rather than its cause.

The mechanics of the heart action are of the same order as in the examples cited above, being a contraction of the walls of a hollow organ upon the contents, expelling them in the direction of least resistance.

2. THE VOLUNTARY MUSCLES.

a. Muscular Organs: The Tongue.

A purely muscular organ like the tongue of one of the higher animals, the proboscis of the elephant, or the prehensile upper lip of the horse and allied animals, notably the tapir, present the most perfect types of universal motion in the animal economy. The tongue may be lengthened or shortened, raised or lowered, swept from side to side, or circumducted at will. The highly mobile and prehensile tongue of the cow may even present various combinations of these movements in different portions of the tongue.

The movements may be rapid and strong. From the standpoint of mechanics the tongue represents a flexible lever of the third class, whose fulcrum is the base of the tongue and whose weight may be represented by the tip. The power is applied between the fulcrum and the weight by the contraction of the muscles on one side of the lever to turn the tip in that direction. The central portion of the lever would be represented by the relaxed muscles on the convex side of the tongue.

b. Muscle-bone Organs: The Skeletal Muscles.

Muscle alone or bone alone could not accomplish locomotion or any of the general movements of the body. A locomotory organ among the vertebrates has two essential components, viz., muscle and bone. The so-called skeletal muscular system is a system composed of *muscle-bone organs.*

1. **The General Functions of Muscle-bone Organs.**—(*a*) **Flexion and Extension** are terms applied to the bending and the unbending of segments of the body or of its appendages. For example, the forearm may be flexed upon the upper arm, and then straightened out or extended. The fingers are flexed when one grasps an object and extended when one releases the object. The thigh may be flexed upon the abdomen, the leg may be flexed upon the thigh, and the foot may be flexed upon the leg.

(*b*) **Adduction and Abduction** are terms applied to the carrying of arms or legs toward or away from the median ventral plane of the body.

The confusion which exists in the application of some of these terms, especially of abduction, adduction, flexion, and extension of arm, necessitates their further illustration. To that end let us recall the general disposition of the muscle-bone organs in a typical mammal. (See Figs. 293 and 294.)

Adduction is the bringing of the femur or humerus toward the median ventral plane of the body, or the bringing of a digit toward the axis of the pes or the manus. Abduction is motion in the opposite direction. Man in his erect position with the arms held in the horizontal plane laterally may bring them toward the median ventral plane, keeping them in the horizontal plane—*Ventral Adduction of the Humerus;* or he may bring them to the same median plane above the head—*Anterior Adduction of the Humerus;* or he may bring them down to the sides—*Lateral Adduction of the Humerus.* In a similar manner there may be *Posterior and Ventral Adduction of the Thigh or Femur,* but, except in the case of contortionists, the hip-joint will not admit of lateral adduction. When the typical mammal stands upon all-fours the anterior and posterior extremities of one side define a ventral plane. In flexion the femur moves anteriorly in that plane until, in extreme flexion, it rests upon the abdomen. The humerus in flexion moves posteriorly in the vertical plane until, in extreme flexion, it rests against the thorax or slides along the thoracic wall until its axis approaches or even passes a line parallel to the axis of the body. In man, when in the erect position, with the arms extended horizontally in front (ventrally) and parallel to each other, the arms would be flexed upon the body by bringing them down to the thoracic walls, keeping them in the vertical plane throughout the movement.

(*c*) **Rotation.**—Certain joints, notably the ball-and-socket joints at the proximal extremities of humerus and femur, admit of a rotation of the limb about its axis. If one rests the weight upon the heel the toe may be swung to right or left through an angle of about 90 degrees. It is neither the ankle-joint nor the knee-joint which moves in this case, but the hip-joint, the head of the femur rotating readily within the acetabulum of the innominate bone. In a similar way the arm may be rotated upon its axis through the rotation of the head of the humerus in the glenoid cavity of the scapula. Another rotating articulation is found between the two bones of the forearm; the radius, rotating upon the external condyle of the humerus, is thrown obliquely across the ulna in *pronation* and drawn back parallel to the ulna in *supination*. Under the head of rotation one may enumerate: (I) rotation proper; (II) pronation and supination.

FIG. 293

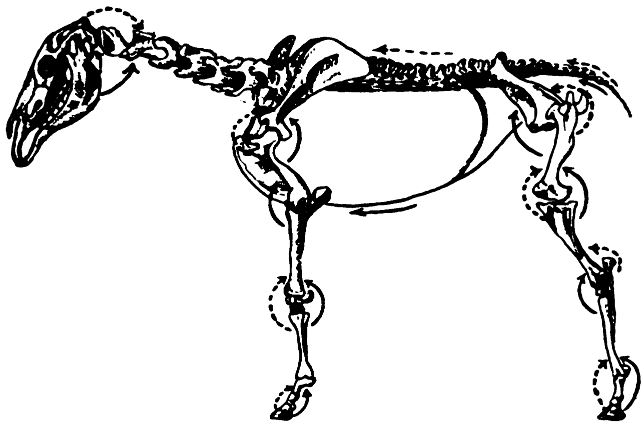

FIG. 294

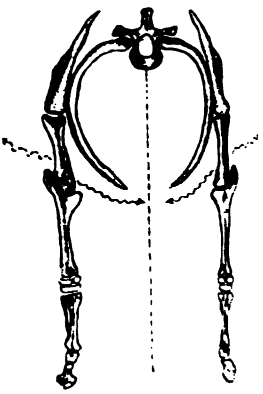

Diagram of typical mammalian skeleton.

——> Flexion, ·········> Extension, ~~~> Adduction, ·~·~·~·> Abduction.

(*d*) **Circumduction.**—All joints which are subject to the four motions, flexion, extension, adduction, and abduction, are subject also to the movement called *circumduction*. One may swing the arm or the leg around in a circle; this is circumduction, and it is clearly a combination of the four motions just enumerated. The muscles and nerves involved in such a motion are simply a combination of those involved in the four primary movements taken together.

What muscles are involved in the above enumerated functions? What is the innervation of the muscles? Through which spinal nerve does the innervation come? Opposite which spinous process is the deep origin of the enumerated nerves? Whence comes the blood supply of the muscles? All of these questions are of importance to the clinician. They are briefly answered in the following table, the data for which have been taken from Quain, Edinger, and Gowers:

2. **Special Functions of Muscle-bone Organs.**—(*a*) MOTIONS OF THE CRANIUM UPON THE SPINAL COLUMN.

FUNCTION.	MUSCLE.	INNERVATION.	NERVE ROOT.	SEGMENT OF CORD.
Flexion	Rectus Cap. Ant. Maj.	Suboccipital	I C	Bet. Occ. & At.
	Rectus Cap. Ant. Min.	"	I II C	Bet. Ax. & Atl.
	Sterno-Cledo. Mast.	Spinal Accessory	XI Cran	Jug. Foram.
		Deep br. of Cerv. Pl.	II C	Body 2d Cer.
Extension.	Rectus Cap. Post. Maj.	Suboccipital	I C	Bet. Occ. & At.
	Rectus Cap. Post. Min.	"	"	" " " "
	Sup. Oblique	"	"	" " " "
	Complexus Bivent.	"	"	Bet. Ax. & Atl.
		Gt. Occipital	II C	Opp. body 2 C.
		Int. Br. Post. Div. Cer.	6–7–8 C	Opp. 4–5–6 C. Sp.
	Splenius Cap. Colli	Ext. Br. Post. Div. Cer.	2–3 C	Bet. Ax. & At.
	Upper seg. Trapezius	Spinal Accessory.	XI Cran	Jug. Foram.
		Ant. Div. 3–4 C.		Opp. 1–2 C. Sp.
Abduction and Adduction.	Recti Lateralis	Suboccipital	I C	Bet. Oc. & At.
	Assisted by: Trapezius	Spinal Accessory	II C	Jug. Foram.
		Ant. Div. 3–4 Cerv.	3–4 C	Op. 1–2 C. Sp.
	Splenius	Ext. Br. Post. Div. Cer.	2–3 C	Op. Bod. 2 [1 C. Sp.]
	Complexus Bivent	Suboccipital	1 C	Bet. At. & Ax.
		Gt. Occipital	2 C	Opp. Bod. 2 C.
		Int. Br. Post. Div. Cer.	6–7–8 C	Op. 4, 5, 6 C. Sp.
	Sterno-Mastoid	Spinal Accessory	II C	Jug. Foram.
		Deep Br. Cer. Plex.	2 C	Opp. Bod. 2 C.
Rotation.	Sterno Mastoid	Deep Br. Cerv. Plex.	2 C	Op. Bd. 2 C.
	Compl. Biv. of one side acting with it.	Suboccipital	1 C	Bet. At. & Ax.
		Gt. Occipital	2 C	Op. Bd. 2 C.
		Int. Br. Post. Div. Cer.	6–7–8 C	4–5–6 C. Sp.
	Rect. Cap. Ant. Maj.	Suboccipital	1 C	Bet. At. & Ax.
	Splenius	Ext. Br. Post. Div. Cer.	2–3 C	Op. Bd. 2 C. [1 C. Sp.]
	Trachelo Mast.	"	"	" "
	Rect. Cap. Post. Maj.	Suboccipital	1 C	Bet. At. & Ax.
	Inf. Oblique	"	"	" "
		Gt. Occipital	2 C	Op. Bd. 2 C.

(β) MOVEMENTS OF THE UPPER ARM.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion	Latissimus Dorsi	L. Subscapular	7 C	Bet. 5–6 C. Sp.	Axillary
	Teres Major	Subscapular	7 C	Bet. 5–6 C. Sp.	"
	Post. Seg. of Delt.	Circ. Br. Cerv. Pl.	4–5 C	Op. 2–3 C. Sp.	Post. Circum.
	Coraco-brach.	Musculo Cutan.	5–7 C	Op. 3 C. Sp.	Brachial
Extension.	Pectoralis Maj.	Ant. Thr. Br. C. Pl.	7 C	Bet. 5–6 C. Sp.	Axillary
	Ant. & Mid. Sg. Del.	Circumflex	4–5 C	Bet. 2–6 C. Sp.	Ant. Circum.
	Coraco-brach.	Musculo Cutan.	5–7 C	Op. 3 C. Sp.	Brachial
	Supra-Spinatus	Supra-scapular	5–6 C	Bet. 4–5 C. Sp.	Post. & Supra Sp.
Lateral Adduc'n.	Pect. Maj. low ⅓	Ant. Thoracic	7 C	Bet. 5–6 C. Sp.	Axillary
	Latissimus Dorsi	L. Subscapular	7 C	"	"
	Teres Maj.	Musc. Br. Subsc.	6–7	"	"
	Long Hd. Triceps	L. Br. Circum.	4–7 C	5–7	"
	Coraco-brach.	Musculo Cutan.	5–7 C	4–5–6	Brachial
Lat. Abd.	Ant. & Mid. Sg. Del.	Upper Br. Circum.	4–5 C	Bet. 2–6 C. Sp.	Circumflex
	Supra-spinatus	Supra-scapular	5–6 C	5–6	Post. Supra Sp.
	Infra-spinatus	" "	5–6 C	5–6	" "
Ventral Adduc'n.	Pect. Maj. Upper Pt. until horizontal then low pt. acts	Ant. Thoracic External and Internal	7 C	Bet. 5–6 C. Sp.	Axillary
	Subscapularis	Subscapular	4–8 C	Bet. 5–6 C. Sp.	Subscapular
	Coraco-brachialis	Musculo Cutan.	5–7 C	5–6	Brachial
Ven. Abd.	Post. Seg. Deltoid	Sup. Br. Circum.	4–5 C	Bet. 2–6 C. Sp.	Post. Circum.
	Infraspinatus	Supra-scapular	5–6 C	5–6	Subscapular
	Teres Minor	Br. of Circum.	4–5 C	5–7	Axillary

(γ) MOVEMENTS OF FOREARM.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion.	Biceps	Musculo Cutaneous	5–6 C	Op. 3 C. Sp.	Brachial
	Brachialis Ant.	Br. Musculo Spiral	4–8 C	Bet. 3–6 "	Brachial
		Br. Musculo Cutan.	"	Op. 3 "	Brachial
	Supinator Long	Br. Musculo Spiral	"	Bet. 3–6 "	Radial
	Flex. Carp. Rad.	Br. Musc. Sp. Med.	"	3–6 "	Radial
	Flex. Carp. Ulnar	Ulnar.	8 C 1 D	Op. 6–7 "	Ulnar
	Flex. Sub. Dig.	Musc. Br. Median	4–8 C	Bet. 3–6 "	Ulnar & Med.
Extension.	Triceps	Musculo Spiral	4–5 C	Bet. 3–6	Brachial
	Anconeus	" "	"	3–6	Brachial
	Ext. Carp. Rad. Long	" "	"	3–6	Radial
	Ext. Carp. Rad. Brev.	Post. Interosseous	"	3–6	Radial
	Ext. Carp. Ulnaris	" "	"	3–6	Ulnar
Supination.	Supinator Long.	Musculo Spiral	4–7 C	Bet. 3–6 C. Sp.	Radial
	Supinator Brev.	Post. Interosseous	"	3–6	"
	Biceps	Musculo Cutaneous	"	3–6	Brachial
	Flex. Carp. Rad.	Median	"	3–6	Radial
Pronation.	Pronator Rad. Ter.	Ant. Thoracic	8 C 1 D	5–6	Rad. & Ulnar
	Pronator Quadratus	Median	5–8 C	5–6	Rad. & Ulnar

(δ) MOVEMENTS OF THE HAND.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion	Flex. Carp. Ulnar	Ulnar	8 C 1 D	Op. 6–7 C. Sp.	Ulnar
	Palmaris Brev.	Median	4–8 C	Bet. 5–6	"
	Palmaris Long.	Median	"	5–6	"
	Finger Flexors	Median & Ulnar	8 C 1 D	Op. 6–7	Ulnar. Rad. Med.
Extension.	Ext. Carp. Rad. Long	Musculo Spiral	4–7 C	Bet. 3–6	Radial
	Ext. Carp. Rad. Brev.	Post. Interos.	"	3–6	"
	Ext. Carp. Ulnaris	" "	"	3–6	Ulnar
	Finger Extensors	" "	"	3–6	Ulnar. Rad. Med.

(ε) MOVEMENTS OF THIGH.

FUNCTION.	MUSCLE.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion.	Psoas Magnus	1-2 Lumbar	3-4 L	Op. 11 D. Sp.	Ilio Lumb.
	Iliacus	Ant. Crural	6 L	Bet. 11-12	Obt. Glut.
	Adduct. Long.	Obturator	1-4 L	Op. 12	Ob. Gl. Int. C.
	Adduct. Brevis.	Obturator	"	"	" " " "
	Sartorius	Ant. Crural	6 L	Bet. 11-12	Br. Prof. Fem.
	Pectineus	Ant. Crur. & Obt.	Above	Above	Ob. Gl. Int. C.
	Gracilis	Ant. Crur. & Obt.	"	"	" " " "
	Rectus Femoris	Ant. Crural	"	"	Br. Prof. Fem.
	Tensor Vag. Fem.	Supt. Gluteal	1-4 L	Op. 1 L. Sp.	Ext. Circum.
Extension.	Gluteus Max.	Sup. Gluteal S. Sc.	Above	Above	Scitaic. Glut.
	Gluteus Med.	" "	"	"	Prof. Fem.
	Gluteus Min.	" "	"	"	" "
	Biceps Fem.	" "	"	"	" "
	Semimembranosus	" "	"	"	" "
	Semitendinosus	" "	"	"	" "
Adduction.	Adduct. Mag.	Sup. Glut. Br.Gt.Sc.	1-4 L	Above	Ob. Gl. Int. C.
	Adduct. Long.	" "	Above	"	" " " "
	Adduct. Brev.	" "	"	"	" " " "
	Pectineus	Ant. Crural	"	"	" " " "
	Gracilis	Obturator	"	"	" " " "
Abduction.	Glut. Medius	See above	Above	Above	Gluteal.
	Glut. Minimus	" "	"	"	"
	Tens. Vag. Fem.	" "	"	"	Ext. Circum.
Rotat'n outw'd.	Pyriformis	Br. from Sacral	1-4 L	Op. 1 L. Sp.	——
	Gemelli inf. et Sup.	" " "	"	"	——
	Obturator int. et Ext.	Obst. & Br. from Sc.	1-4 L	"	——
	Quadratus Femoris	5th humb. 1st Sc.	"	"	——
Rotat'n inw'd.	Glut. Med. (ant. bun.)	See above	——	——	——
	Glut. Min. " "	" "	——	——	——

(ϛ) MOVEMENTS OF LEG AND FOOT.

FUNCTION.	MUSCLES.	INNERVATION.	NERVE ROOT.	SEG. OF CORD.	BLOOD SUPPLY.
Flexion of Leg (crus.).	Biceps Femoris	Sup. Glut. S. Scia.	2-3 L	Op. 1 L. Sp.	Prof. Femoris
	Semimembranosis	" " " "	"	"	" "
	Semitendinosis	" " " "	"	"	" "
	Popliteus	Int. Popliteal	3-4 S	"	Pr.Fem. Post.Tb.
	Gracilis	Obt. Br. Gt. Sciat.	Abv.	"	Prof. Fem.
	Sartorius	Ant. Crural	6 L	"	Popliteal
	Gastrocnemius	Int. Popliteal	Abv.	"	Post. Tib.
Ext. of Leg (crus.).	Rectus Femoris	Ant. Crural	Abv.	Bet. 11-12.	Prof. Fem.
	Vastus Externus	" "	"	"	" "
	Vastus Internus	" "	"	"	Anast. Mag.
	Crureus	" "	"	"	Pop. Pro. Fem.
Flex. of foot.	Tibialis Anticus	Ant. Tibial	Abv.	Bet. 11-12.	Ant. Tibial
	Peroneus Tertius	" "	"	"	Peroneal
	Ext. Long. Dig.	" "	"	"	Ant. Peron.
	Ext. Prop. Hallucius	" "	"	"	Ant. Tibial
Extension of foot.	Gastrocnemius	Int. Popliteal	Abv.	Bet. 11-12.	Post. Tib.
	Soleus	" "	"	"	Peroneal
	Tibialis Post.	Post. Tibial	1-2 L	"	Post. Tib.
	Peroneus Longus	Musculo Cutan.	4-5 L	"	Peroneal
	Peroneus Brevis	" "	"	"	"
	Plantaris	Int. Popliteal	Abv.	"	"
	Flex. Long. Dig.	Post. Tibial	"	"	Post. Tib.
Lateral. ab.	Tibialis Posticus	Post. Tibial	Abv.	Bet. 11-12.	Post. Tib.
	Peroneus Brevis	Musculo Cutan.	"	"	Peroneal
Lateral. add.	Ext. Long. Hallucius	Ant. Tibial	Abv.	Bet. 11-12.	Ant. Tibial
	Tibialis Anticus	" "	"	"	" "

In the compilation of the above table it was found that the statements of Gray, Quain, and other anatomists do not agree as to the function of particular muscles. In all such cases the author has accepted the authority of *Duchenne*, whose classic work, "*Physiologie des Mouvements*," still remains without an equal.

3. **Animal Mechanics.**—Animal mechanics is the application of the laws of mechanics to animal motion. The bones are used as levers; the articular surfaces of bones usually serve as fulcrums, while the power is exerted by the muscles. In a vast majority of cases the bones represent levers of the third class—in which rapidity of motion is attained at the expense of power. In other words, the arrangement of the bone-muscle organs is such that a contraction of a muscle—moderate in extent and rate of motion—is manifested by a movement of the limb which is much in excess, as to extent and rate, of the movement of the power.

In solving problems in animal mechanics the principal factors to be considered are: (I) the relative length of the two lever arms; (II) the relative size of the muscles involved in any movement; (III) the direction in which the power acts, and (IV) the weight to be moved.

(*a*) **Problems in Animal Mechanics.**—Two typical problems in animal mechanics are the following:[1]

1. Determine, in a particular case, the tension exerted upon the tendo Achillis in supporting the weight (60 kilograms) of the subject upon the ball of the foot.

2. How much tension would there be on the biceps tendon in the subject upon your dissecting table when he holds a ten-kilo. iron ball in the most advantageous position? This is a typical problem, and its solution will make the difficulties to be encountered apparent. It will also show that nothing more than an approximate solution can be attained without an extended and detailed study.

Solution.—The principal muscle involved in the required action being the biceps, the most advantageous position is the one in which that muscle exerts its power in a line perpendicular to the lever. Placing the subject's arm as nearly as possible in that position, one takes the following measurements: (I) The long arm of the lever: this would be from the centre of articulation between the humerus and the ulna, to the centre of the ten-kilo. ball, which would be, approximately, to the distal extremities of the metacarpal bone (36 cm.). (II) The short arm of the biceps lever; this would be the distance from the centre of the insertion of the biceps to the fulcrum —the centre of articulation (6 cm.). (III) The short arm of the lever for the brachialis anticus. If the brachialis anticus were exactly parallel to the biceps the short arm would be the distance from the insertion to the fulcrum (5 cm.), as in the biceps; but it is not parallel.

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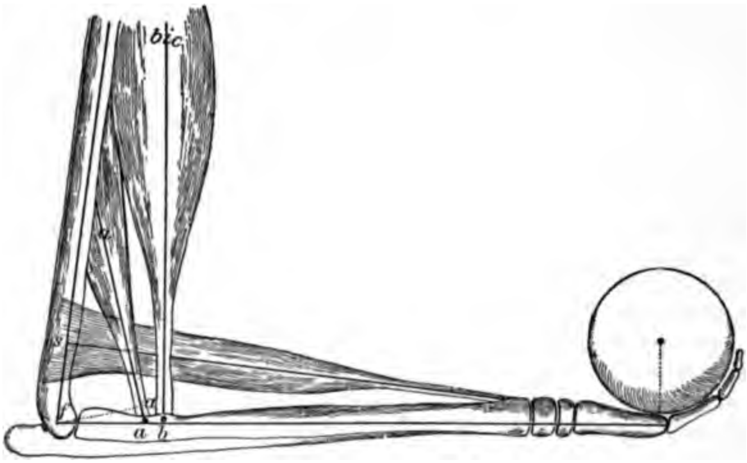
[1] Both of the problems stated above are problems in "muscle statics." Such problems deal with tension upon muscles when the limb is in a certain fixed position. There are much more complicated problems which deal with the energy exerted in a more or less complex movement when the leverages and angles of tension are constantly varying. Such problems in "muscle dynamics" can only be solved by the application of higher mathematics. Otto Fischer, of Leipzig, has done much to throw light into this field of physiology. See his "Beiträge zur Muskelstatik," also "Beiträge zu einer Muskel-dynamik."

A line drawn from the fulcrum perpendicular to the axis of the brachialis anticus, *f a′*, is shorter than the line *f a*. The angle between the brachialis anticus and the biceps is approximately 10 degrees; therefore, the angle *a f a′* would be approximately 10 degrees; then *a′ f* is the cosine 10 degrees or 98 per cent. of the radius *a f* (5 cm.), or 4.9 cm.

(IV) The power-arm of the supinator longus is the perpendicular distance from the fulcrum to the line of force of the supinator longus

FIG. 295



Mechanics of flexion of the forearm. [The upper *a* is to be understood as *a′*.]

and is represented by the line *f s*, which is 4.8 cm. Now the carpal and digital flexors which take origin from the humerus act as forearm flexors after having flexed the carpus and digits. In the action under consideration they would not be brought into forcible action as carpal and digital flexors. We may, therefore, ignore them and confine our discussion to the three muscles mentioned above.

In the action of the biceps the long arm is 36 cm. and the short arm 6 cm.; in the action of the brachialis anticus the long arm is 36 cm. and the short arm 4.9 cm.; in the action of the supinator longus the long arm is 36 cm. and the short arm 4.8 cm. Reducing these to per cent. ratios we have: For the biceps, which we will designate as *b*, 16.6 per cent. leverage; for the brachialis anticus, which we will designate as *a*, 13.6 per cent. leverage; and for the supinator longus, which we will designate as s, 13.3 per cent. leverage.

But there is another important consideration: Fick has demonstrated that when the fibres are parallel the strength of two muscles is proportional to the areas of their cross-sections.[1] The average ratio of the diameter of the three muscles in question is 4 : 2 : 1, respectively; but the areas of the cross-sections would be proportional to the squares of the diameters, or as 16 : 4 : 1, respectively. This means that with the same leverage the biceps would lift four times as much as the brachialis anticus, and that the brachialis anticus would, with the same leverage, lift four times as much as the supinator longus.

We have now discussed the relation of these three factors as to *leverage* and as to *relative power* exerted.

As to leverage one may say: The power of the three muscles varies in proportion to biceps leverage (bl); brachialis anticus leverage (al); supinator longus leverage (sl), respectively; or, mathematically expressed, P varies as $bl : al : sl$, or varies as 16.6 : 13.6 : 13.3. As to cross-section one may say: The power varies in proportion to the respective cross-sections (s) or P varies as $bs : as : ss = 16 : 4 : 1$. Now, when any function varies with two or more variable factors, its variation when influenced by the action of all of these factors at once would be represented by the product of the several variables. Then the power varies as the leverage times the cross-section of each of the muscles when all act together, or, expressed mathematically, P varies as $b(l\times s) : a(l\times s) : s(l\times s)$.

But $b(l\times s) = 16.6 \times 16 = 265.6$, or 79.7 per cent. of the total power exerted; $a(l\times s) = 13.6 \times 4 = 54.4$, or 16.3 per cent. of the total power exerted; $s(l\times s) = 13.3 \times 1 = 13.3$, or 4.0 per cent. of the total power exerted; total $= 333.3$, or 100.0 per cent.

But the weight supported by the action of these muscles is 10 kilos. If the biceps does 79.7 per cent. of the total work, it would support 7.97 kilos. What would be tension upon the tendon of the biceps when it is supporting 7.97 kilos. at the end of its lever? One needs only to use the 16.6 per cent. leverage ($7.97 \div 16.6$ per cent.) to find that the tension would be 47.8 kilos. A similar process shows that the approximate tension upon the tendon of the brachialis anticus is 12 kilos. and upon the tendon of the supinator longus 3 kilos.

(*b*) **The Amount of Contraction of a Muscle** bears a fairly constant ratio to the resting length of the muscle. This law of muscle physiology was discovered and demonstrated by Ed. Fr. Weber[2] and was cited by Strasser[3] as an example of the adaptation of muscle tissue to the mechanical requirements of the body. Weber showed that the maximum contraction of which a muscle fibre is capable is approximately 47 per cent. of its resting length. Both Weber and Strasser looked upon this as the factor which determines the length of the muscles, and the location of their points of origin and insertion. In all of the skeletal muscles the tension of the contracting muscle is greater than the weight lifted. The farther the insertion of a muscle from a joint (fulcrum) the less the tension upon the muscle and the greater the amount of contraction or shortening necessary; but the inherent structure of striated muscle tissue seems to set 47 per cent. as the limit of the extent of its contraction. The fact that all skeletal muscles actually do contract that much (varying however, in special instances from 44 per cent. to 62 per cent.) indicates that the position of the origin and insertion or the length of muscle tissue (excluding tendon) between the origin and insertion; or, more likely, that both of *these structural features have been determined by the laws of selection, and now represent in all highly organized animals the most perfect mechanical adjustment consistent with the inherent properties of muscle tissue.*

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[1] Hermann's Handbuch der Physiologie, vol. i. p. 295.

[2] Mechanik der menschlichen Gehwerkzeuge, 1851.

[3] Funktionellen Anpassung der Quergestreiften Muskeln, 1883.

(c) **Problems in Human Locomotion.** (α) THE MUSCLES USED IN LOCOMOTION.—Let a person stand erect with heels together; let him take several steps forward and stop in a position similar to the one which he had at the beginning. What is the mechanism of *starting?* What muscles are involved in starting? What is the mechanism of *locomotion?* What muscles are involved in locomotion? What is the mechanism of equilibration while walking? What muscles are involved in maintaining the equilibrium while walking? What is the mechanism of *stopping?* What muscles are involved in stopping? How is the equilibrium maintained during the process of stopping? What muscles are involved in the maintenance of equilibrium while standing? How does running differ from walking in the *starting*, the *locomotion*, the *equilibration*, and the *stopping?*

(β) THE ENERGY INVOLVED IN LOCOMOTION.—How far is the body lifted at each step when one walks over a level surface? When one walks up an incline of 30 degrees? When one walks down an incline of 30 degrees? Does one do work while walking down hill? If so, how may it be computed? If not, why does one become fatigued in descending an incline? How much energy will a 70-kilo. man expend in walking 1 kilo. on a level road? (Suppose the man to be 172 cm. in height, and to have a pubic height of 88 cm.) A part of the energy will be expended (I) in lifting the body, (II) a part in maintaining equilibrium, (III) and a part in overcoming resistance. Express in kilogram-metres the amount of energy expended in (I). How could one determine the amount of energy expended in (II)?

DIVISION *C*.

CHAPTER XIII.

REPRODUCTION.[1]

THE PHYSIOLOGY AND MORPHOLOGY OF REPRODUCTION.

1. THE OVUM.
2. MATURATION.
3. FERTILIZATION.
4. SEGMENTATION.
5. THE EMBRYO: HISTOGENESIS.
    - (*a*) The Development of the Germ Layers.
    - (*b*) The Development of the Primitive Segments.
    - (*c*) The Beginning of the Nervous System.
    - (*d*) The Mesenchyme.
    - (*e*) The Origin of the Urinary System.
    - (*f*) Summary of Early Development: Histogenesis.
6. THE FETUS: ORGANOGENESIS.
    - (*a*) The Circulatory System.
    - (*b*) The Respiratory System.
    - (*c*) The Digestive System.
    - (*d*) The Urogenital System.
    - (*e*) The Central Nervous System.
7. THE FETAL ENVELOPES.
    - (*a*) The Fetal Membranes.
    - (*b*) Maternal Portion of Envelopes: Deciduæ and Placenta.
8. THE PHYSIOLOGY OF THE EMBRYO AND FŒTUS.
    - (*a*) Nutrition.
    - (*b*) Motosensory Activity.
9. THE PHYSIOLOGY OF MATERNITY.
    - (*a*) Pregnancy and Parturition.
    - (*b*) Lactation.

THE parental phases of reproduction include all of those activities involved in the production of offspring. Two general phases in the production of offspring are (1) the transmission of hereditary characters and (II) the nourishment and protection of the young during a longer or shorter period of development.

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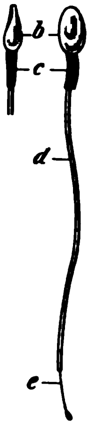
[1] The introduction to the processes of reproduction may be found in Part I., Cellular Biology. It is proposed to give here a very brief summary of mammalian reproduction and development, especially emphasizing the physiologic phases of the processes.

In mammalian reproduction one may profitably consider the following special processes: (I) The *formation* of the germ cells; the *maturation* of the germ cells; the conjugation or fusion of the germ cells (*fertilization*). (II) The *segmentation* of the fertilized ovum; the *intrauterine development* successively, of the blastoderm, the gastrula, the three-layered embryo, and the fœtus; parturition; lactation; *extrauterine* development.

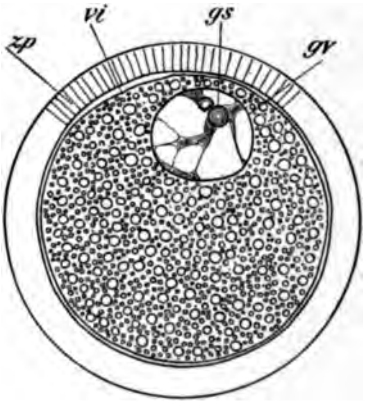
Some of these processes represent activities of the parents; some, those of the developing young.

FIG. 296



Human spermatozoa. × 1000. 1, in profile; 2, viewed on the flat; *b*, head; *c*, middle piece; *d*, tail; *e*, end piece of the tail, which is described as a distinct part by Retzius. (Schäfer, after Retzius.)

FIG. 297



Semidiagrammatic representation of a mammalian ovum. (Highly magnified.) *zp*, zona pellucida; *vi*, vitellus; *gv*, germinal vesicle; *gs*, germinal spot. (Schäfer.)

The paternal portion of the general process consists in the production of the male germ cells and assisting in the nourishment and protection of the young during its extrauterine development. The male reproductive cell—the spermatozoön (Fig. 296)—serves the double purpose (I) of transmitting to the offspring the hereditary characters of the paternal ancestral line, and (II) of inducing in the ovum the process of segmentation.

The maternal portion of the general process consists in the production of the female germ cells and the protection and nourishment of the young during intrauterine development and infancy, and assisting in its nourishment and protection during childhood and youth.

The offspring is passive as an individual during intrauterine life, but its cells and tissues are exceedingly active. The activity takes the form of the following processes: Segmentation, formation of embryonic layers, development of tissues and organs drawing sustenance for these structures from the maternal organism.

Without further following the distinction between parental and embryonic processes we may now summarize the whole process of reproduction and development.

1. THE OVUM.

The ovum is a simple, single cell. The parts of this gigantic cell have received special names: the cell wall is called the *vitelline membrane;* the protoplasm with its reserve nutriment is called the *yolk,* the nucleus becomes the *germinal vesicle;* the nucleolus the *germinal dot* (Fig. 297).

2. MATURATION.

Before the egg is ready to be fertilized the process of maturation takes place in the following manner, in the egg of an echinoderm (Fig. 298, *a* to *g*):

(I) The germinative vesicle gradually moves from the centre of the egg toward its surface, its nuclear membrane disappears, and the germinative dot breaks up into small, hardly visible fragments.

(II) There arises out of a part of the nuclear substance of the germinative vesicle a *nuclear spindle* which pursues still farther the direction taken by the germinative vesicle until it touches with its apex the surface of the yolk, where it assumes a position with its long axis in the direction of a radius of the sphere.

(III) A genuine process of cell division soon takes place here, which is to be distinguished from the ordinary cell division only in this: that the two products *of cell division are* of very unequal size.

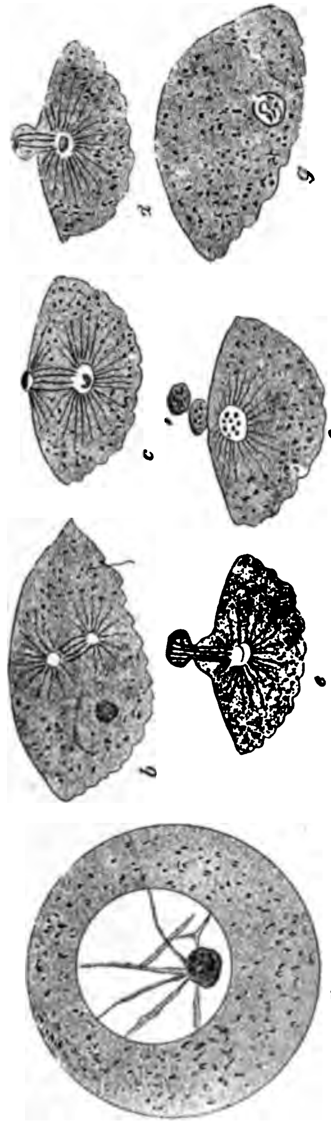
More exactly expressed, this process is a cell-budding (gemmation). This process of gemmation occurs twice. The two small cells are called polar bodies.

(IV) After the conclusion of the second process of budding the remaining part of the spindle, one-fourth of the original spindle, is left in the cortical layer of the yolk. From this arises a new, small, vesicular nucleus, which consists of a homogeneous fluid substance without distinct nucleolus. From its peripheral position it usually migrates slowly back toward the middle of the egg. Thus it completes in four phases the process of maturation. There is no reason to doubt that the process of maturation in the mammalian egg is in any important feature different from that in the egg of the echinoderm.

3. FERTILIZATION.

FERTILIZATION is the union of egg cell and spermatic cell, more technically union of their nuclei; without this union a complete, normal development into the perfect adult form is impossible. The spermatic cell is the male element of reproduction; in most

FIG. 298



Maturation of egg of *Asterias gracilis*: *a*, ovarian egg; *b* and *c*, stages (I) and (II) of maturation; *d* and *e*, stage (III) of maturation; *f* shows polar bodies divided off from the ovum; *g*, mature ovum ready for fertilization: *g f*, the female pronucleus or egg nucleus.

FIG. 299

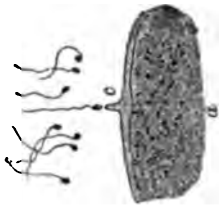


FIG. 300

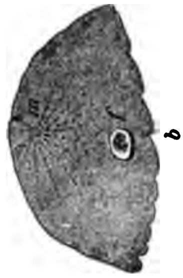


FIG. 301

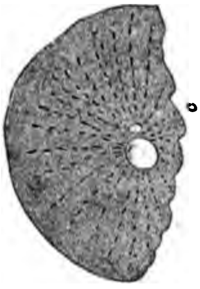
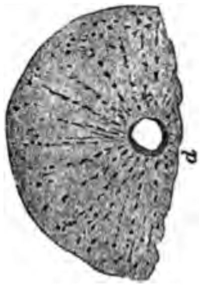


FIG. 302



The process of fertilization in *Asterias*: *a*, the spermatozoa gathering about the attraction cone (c), stage (I); *b*, stage (II), showing male (*m*) and female (*f*) pronuclei; *c* and *d*, stage (III); *d s*, the segmentation nucleus. (After Hertwig.)

animals, both vertebrate and invertebrate, the sperm cell is a flagellate cell whose head represents the nucleus and whose flagellum represents the protoplasm. The male element being the active one in reproduction, the flagellum serves as a locomotory organ (Figs. 298 and 299).

Fertilization may take place within the body of the female or external to it—*internal* or *external fertilization.* (Internal: most vertebrates. External: fishes, amphibia, and most invertebrates).

(I) At fertilization only a single spermatozoön penetrates a sound egg, which occurs at the apex of the cone of attraction.

(II) The head of the spermatozoön is converted into the spermatic nucleus, around which the neighboring protoplasmic granules are radially arranged (Fig. 300).

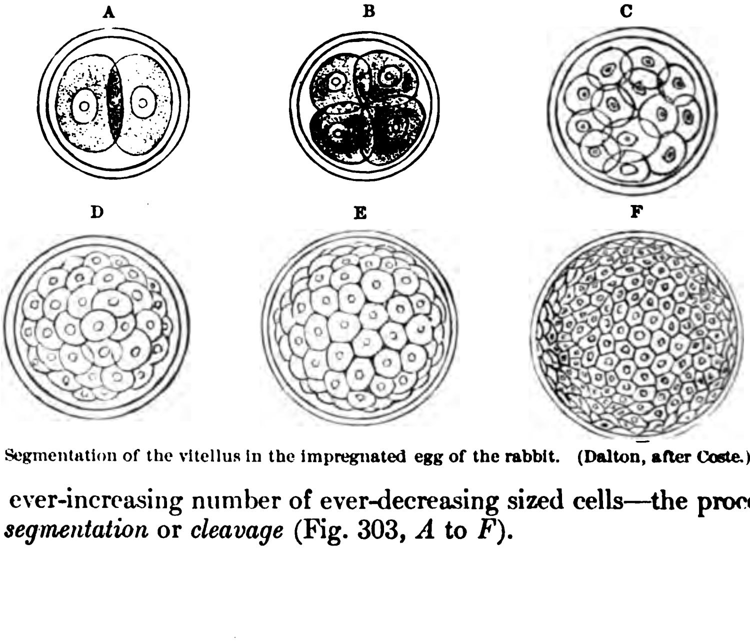
(III) The egg nucleus and spermatic nucleus migrate toward each other and in most instances immediately fuse to form the *segmentation nucleus* (Figs. 301 and 302).

Fertilization depends on the copulation of two cell nuclei which are derived from the male cell and a female cell. The male and female nuclear substances contained in the spermatic nucleus and egg nucleus are bearers of the peculiarities which are transmissible from parents to their offspring.

4. SEGMENTATION.

Fertilization is in most cases immediately followed by further development which begins with the division of the egg cell into an ever-increasing number of ever-decreasing sized cells—the process of *segmentation* or *cleavage* (Fig. 303, *A* to *F*).

FIG. 303



Segmentation of the vitellus in the impregnated egg of the rabbit. (Dalton, after Coste.)

(*α*) Internal Phenomena of Segmentation. 1st. *The cleavage nucleus*, at first spheroidal, forms the centre of a radiation which affects the whole yolk mass, but it soon begins to be slightly elongated, to become less and less distinct. The monocentric radiation is divided; the two newly formed radiations thereupon move to the poles of the elongated nucleus; they rapidly separate and finally each occupies a half of the egg.

The nucleus while in the process of division consists of an *acromatic* and a *chromatic* figure—the former a spindle composed of a definite number of fibres, the latter the same number of V-shaped nuclear segments—chromosomes, which lie upon the surface of the middle of the spindle. 2d. The chromosomes split lengthwise and their halves move in opposite directions, apex first, to the polar centrosomes, where they form the daughter stars, later the daughter nuclei.

(*β*) External Phenomena of Segmentation consist in the division of the egg contents into cells, the number of which correspond to the number of nuclei.

5. THE EMBRYO.

Beginning with a single *cell*—the egg cell—we have followed the development of a mass of cleavage cells—the morula, blastula, of which there are four forms.

a. The Development of the Germ Layers.

1. **The Blastula,** *with one germ layer.*

(*α*) In Amphioxus the cleavage cavity is very large and its wall consists of a single layer of cylindric cells of nearly uniform size (Fig. 304, *a*).

(*β*) In Amphibia the cleavage cavity is small; the wall consists of a thin pole composed of small cells and a thick pole composed of several layers of large cells (Fig. 300, *b*).

(*γ*) In Fishes, Reptiles, and Birds the cleavage cavity is fissure-like or wanting; the roof is the germ disk and the floor is the yolk mass, which is not divided into cells (Fig. 306, *c*).

(*δ*) In Mammals—Man—the cleavage cavity is spacious and filled with albuminous fluid; the wall is a single layer of hexagonal cells, with the exception of one pole, whose larger cells in a mass extend into the cavity.

2. **The Gastrula,** *with two germ layers.* The invagination of the blastula forms the two layers of the gastrula; the outer layer is the *ectoderm* or *epiblast;* the inner layer is the *entoderm* or *hypoblast;* the cleavage cavity is obliterated; the invagination cavity is the cœlenteron, its external mouth the primitive mouth, *blastopore, primitive groove,* or *prostoma.*

(α) IN AMPHIOXUS the blastopore is large, the cœlenteron capacious, each germ layer composed of a single sheet of cylindrical cells (Fig. 307).

(β) IN AMPHIBIA the blastopore is small, the mass of yolk cells is ventral to the cœlenteron, which is arched upward and is fissure-like (Fig. 308).

(γ) IN FISHES, REPTILES, AND BIRDS the blastopore is crescentic; the germinal disk becomes two-layered by means of ingrowth of cells from the blastopore. The cœlenteron is ventral to the lower layer of cells—*i. e.*, it is ventral to the hypoblast (Fig. 309).

FIG. 304

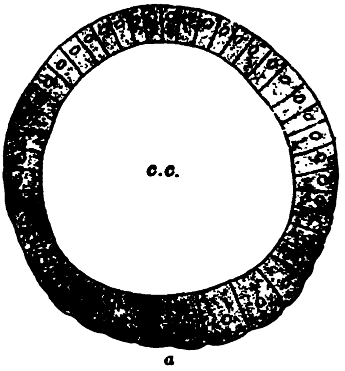


FIG. 305

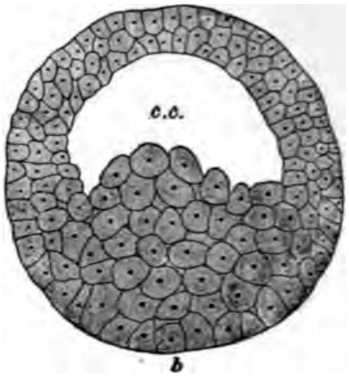
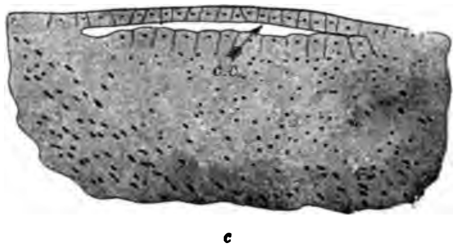


FIG. 306



The process of blastulation. *a*, blastula of *Amphioxus*; *b*, blastula of triton (amphibian); *c*, blastula of bird; *c. c.*, cleavage cavity. (After Hertwig.)

(δ) IN MAMMALS the blastopore is minute and circular, and over a thickened pole the cœlenteron and cleavage cavity are one and the same cavity.

In all vertebrates the gastrula presents bilateral symmetry and anteroposterior differentiation; the blastopore is always posterior—dorso ventral differentiation—and the yolk mass is always ventral.

3. **The Embryo,** *with three germ layers.*

In all vertebrates there are formed from the roof of the cœlenteron two lateral evaginations of the inner germ layer or hypoblast, by means of which the cœlenteron is divided into a median cavity—the intestine—and two lateral cavities, cœlomic cavities, or body cavities. The *primary* inner germ layer thus becomes differentiated

FIG. 307

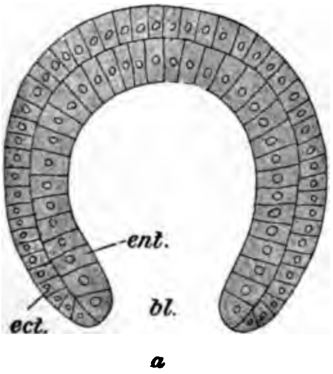


FIG. 308

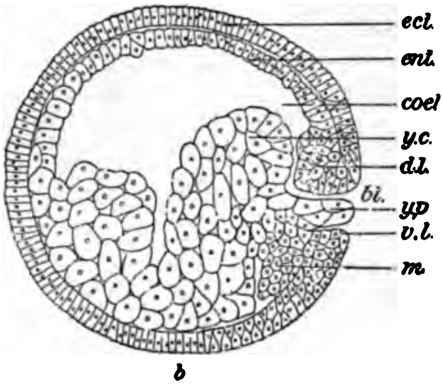
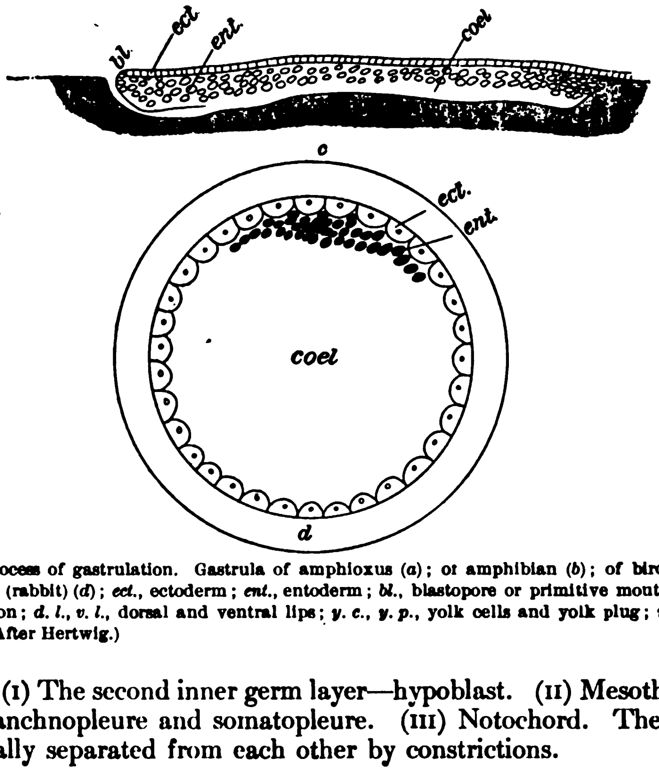


FIG. 309



The process of gastrulation. Gastrula of amphioxus (*a*); of amphibian (*b*); of bird (*c*); of mammal (rabbit) (*d*); *ect.*, ectoderm; *ent.*, entoderm; *bl.*, blastopore or primitive mouth; *coel.*, cœlenteron; *d. l.*, *v. l.*, dorsal and ventral lips; *y. c.*, *y. p.*, yolk cells and yolk plug; *m*, mesoblast. (After Hertwig.)

into: (I) The second inner germ layer—hypoblast. (II) Mesothelium of splanchnopleure and somatopleure. (III) Notochord. These are gradually separated from each other by constrictions.

The development—*i. e.*, differentiation of the mesoblastic plates—takes place from before backward while the growth takes place at the blastopore, thus pushing the embryonal layers forward from that point. During the growth of the mesoblast the blastopore has been metamorphosed into the primitive groove (Figs. 310 and 311). The primitive groove undergoes degeneration and is not converted into any organ in the adult.

Fig. 310

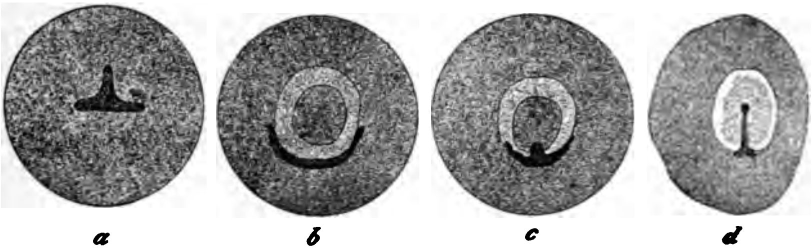
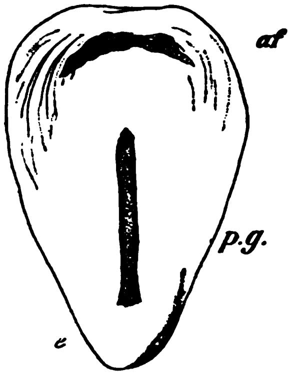
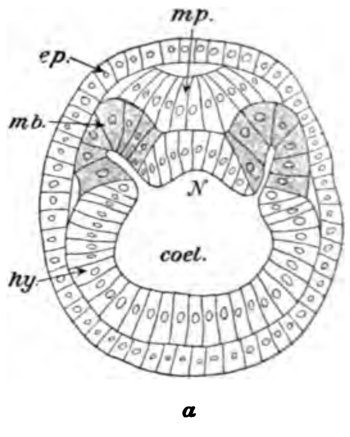


Fig. 311



The form of the blastopore and its metamorphosis in the chick embryo: *a*, blastopore of triton; *b* to *e*, blastopore of a chick gradually transformed from a transverse crescentic slit to a longitudinal groove—the primitive groove (*e.*, *p. g.*). (After Hertwig.)

Fig. 312



b. The Development of the Primitive Segments.

In the mammals, birds, reptiles, amphibians, and fishes the mesoblast first appears as lateral somatic and splanchnic plates. At the time when these are constricted off from the cœlenteron the free edges fuse and immediately thicken along the dorsum either side of the notochord. This thickened plate is the *primitive segment plate.* Immediately after formation this segment plate begins segmentation, first in the trunk (30 to 50) and later in the head, eleven in number (Figs. 312 to 316).

c. The Beginning of the Nervous System.

The central nervous system of vertebrates is one of the first to be established after the separation of the germ into the three primitive layers—epiblast, mesoblast, and hypoblast. It is developed out of a broad band of the epiblast, the medullary plate, which lies in the median line just over the notochord. Along this band the epiblastic cells become elongated and cylindric, while the remaining epiblast is composed of flattened plates joining by their edges. An evagination of the margins of the band forms the dorsal folds or *medullary folds.* A continuation of the evagination and a coalescence of the edges of the folds accomplishes a closure of the *neural tube* (Figs. 312 to 315).

FIG. 313

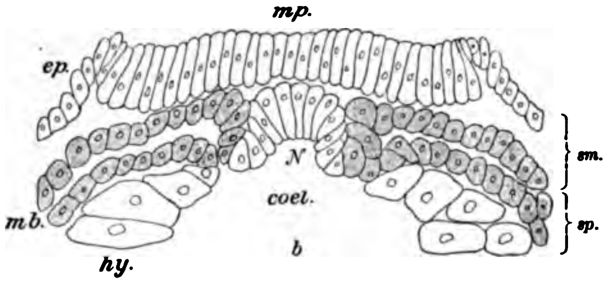
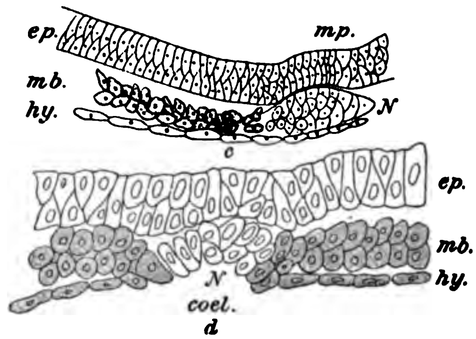


FIG. 314

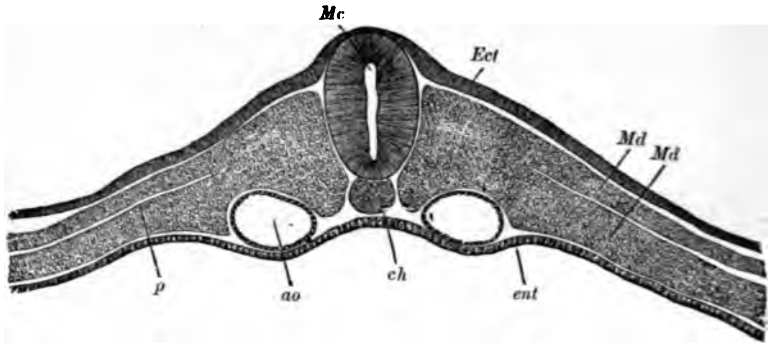


The derivation of the mesoblast and notochord from the primary inner germ layer (hypoblast). Cross-section of the amphioxus (308); of an amphibian (309); of a bird, 310), and of a mole (mammal) (*d*); *ep.*, epiblast; *mb.*, mesoblast; *hy.*, hypoblast; *coel.*, cœlenteron; *N*, notochord. Note that in the amphibian (*b*) the mesoblast is pretty clearly divided into somatopleuric (*sm.*) and splanchnopleuric mesothelium (*sp.*). (Hertwig, after Balfour, Heape, *et al.*)

The part of the neural tube which forms the brain becomes segmented early in the second day of incubation, twenty-fourth to thirtieth hour in the chick, into three primary brain vesicles: (I) the *primary forebrain vesicle,* (II) the *midbrain vesicle,* (III) the *primary hindbrain vesicle.* Between the thirtieth and thirty-sixth hour of incubation the primary forebrain vesicle gives off two lateral evaginations—the *optic vesicles*—and the primary hindbrain vesicle becomes divided into the *cerebellar vesicle* and the *medullar vesicle.* The closure of the neural tube or canal begins at the midbrain and progresses anteriorly over the forebrain and posteriorly over the cerebellar and medullar vesicles and proceeds along the spinal cord, finally closing it in at the posterior end (Fig. 315).

Now it will be remembered that the blastopore, by virtue of the metamorphosis of the crescentic fold is now located at the anterior end of the primitive groove. The closing of the neural canal posteriorly includes the anterior end of the primitive groove with the blastopore. It thus transpires that the blastoporic canal forms a direct communication between the neural canal and the cœlenteron or alimentary canal. This connection persists some time and is known as the *neurenteric canal.* It finally becomes obliterated through fusion of its walls. Thus the last vestige of the blastopore of the higher vertebrates becomes extinct in the early stages of embryonic development.

Fig. 315



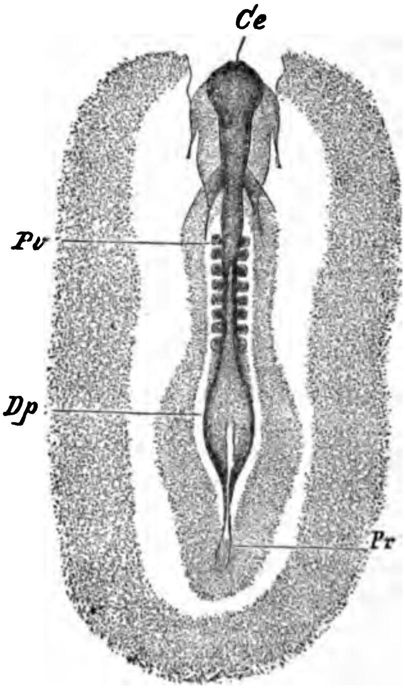
Transverse section of the embryo chick, through closed portion of medullary canal. *Mc.* medullary canal; *Ect,* ectoderm; *ent,* entoderm; *Md, Md',* outer and inner laminæ of mesoderm; *p,* peritoneal space; *ch,* chorda dorsalis; *ao,* aorta. (Kölliker.)

d. The Mesenchyme.

Soon after the formation of the primitive segments, these, which are at first solid, soon acquire a small cavity around which the cells are arranged into a continuous epithelium. The part of the wall lying at its lower median angle begins to grow with extraordinary rapidity and to furnish a mass of embryonic connective tissue which spreads itself around the cord and neural tube (Hertwig). Out of the dorsal and lateral parts of the primitive segment arises the trunk musculature. The *mesenchyme* arises from three other parts of the mesoblast besides the primitive segments, viz., (I) splanchnic mesothelium, (II) somatic mesothelium, and (III) that wall of the primitive segment turned toward the epiblast. These four origins of the mesenchyme justify a classification of this important embryonic structure as (I) *axial mesenchyme,* (II) *splanchnic mesenchyme,* (III) *somatic mesenchyme,* and (IV) *dermal mesenchyme.*

The method by which the mesenchyme arises is peculiar: (I) there is a rapid growth of the cells at some point in the mesoblast, accompanied by (II) a vigorous amœboid movement. This combination makes invagination or evagination of a body of cells a mechanical impossibility; instead of that process, *individual cells* leave the parent epithelium and, by virtue of their continued amœboid movements, wander between the somatopleure and epiblast or between the splanchnopleure and hypoblast, as the case may be. The origin and destiny of the mesenchyme have been for more than a decade a riddle whose solution has engaged the attention of His, Kölliker, Heape, Waldeyer, and other embryologists.

FIG. 316



Embryo chick, about the fortieth hour of incubation: *Ce*, cephalic extremity; *Pv*, primitive segments or protovertebræ; *Dp*, dorsal plates still widely separated in the caudal region; *Pr*, primitive groove. (Kölliker.)

At the time of the formation of the mesenchyme—end of first day in the chick—two necessities begin to press themselves upon the developing organisms: (I) necessity for mechanical support, and (II) necessity for nutrition. The first of these necessities urges itself upon the axial part of the embryo, for there the delicate nervous system is passing rapidly through the steps of its development. The need for nutriment will not be felt by the epiblast or by the hypoblast, for these layers are next to the supply of nourishment; but by the mesoblast, in contact with neither white nor yolk. It is a law of biology that *hungry organisms* ,*are restless*, while satiated organisms are sluggish. Recall at this point the fact that the mesoblast cells which form the somatopleuric and splanchnopleuric mesenchyme *free themselves* from the mesoblast by dint of amœboid movements. These restless hungry cells are out foraging. The leukocytes of the adult body are the descendants of these restless, hungry, foraging cells of the primitive mesenchyme. How are the two necessities mentioned above satisfied?

(*α*) THE NECESSITY FOR SUPPORT for the axial nervous system is satisfied by the *axial mesenchyme* which closes about the central nervous system and the notochord, and later *develops into the axial skeleton* with *all its associated connective tissue.*

(*β*) THE NECESSITY FOR NUTRIMENT is solved by the somatopleuric and splanchnopleuric mesenchyme in the following manner, as represented by Kölliker and subscribed to by Hertwig: "At the end of the first day of incubation the masses of cells which represent the mesenchyme arrange themselves in cylindric or irregularly limited cords which join themselves together into a close-meshed network; they are the first fundaments, both of the bloodvessels and of their contents—the blood. In the spaces of the network are to be found groups of indifferent cells which afterward become *embryonic connective tissues.*" In the beginning of the second day of incubation the "cords" acquire an internal cavity and become bounded superficially by a single layer of flattened polygonal cells—the future endothelium of the bloodvessels. "The cavity of the vessel is probably formed by the penetration of fluid into the originally solid cord, thus forming the plasma of the blood by which the cells are pressed apart," some of these forming the vessel wall, some remaining floating in the fluid and becoming the leukocytes and red blood corpuscles. The red blood corpuscles originate, at the first, in the vascular area of the yolk, from yolk nuclei. They are nucleated during the early embryonic life of mammals and man and increase in numbers rapidly by division.

c. The Origin of the Urinary System.

Before the activities of life begin to make themselves manifest by the expenditure of energy, as in the transportation of matter through space—*e. g.*, the action of the heart walls in the circulation of the blood—there is no need of an excretory system. If we admit, then, that the need for an excretory system arises during the third day in the chick, to what shall we attribute the actual appearance, during the second day, of a rudimentary urinary system? It must be attributed to HEREDITY. It is generally admitted that the genealogy of vertebrates extends through truncates back to worms. From your studies in zoölogy you recall the segmental organs of the higher worms. A pair is located in each segment and each segmental organ is composed of (I) a ciliated funnel, (II) a convoluted tubule, (III) a glandular segment, and (IV) a muscular bladder which opens externally. But this segmental arrangement of the excretory organs is an expensive and clumsy solution of the matter. In the lower vertebrates we see the following improvements: The uriniferous tubules are segmental, but instead of opening individually on the surface of the animal, as in worms, there is a collecting tube which transfers the secretion of all the tubules of one side of the body to a posterior and ventral orifice opening near or into the cloaca. In all the higher vertebrates, including man, the *primitive kidney* or *pronephros is a segmental organ,* and is quite rudimentary, never performing the function of excretion, even in the embryo. "THE PRONEPHROS of the chick is located between the seventh and eleventh somites. The pronephric duct, at its first appearance, is a short, canal-like perforation of the wall of the body, which begins in the body cavity with one or several ostia and opens out upon the skin with but a single external orifice. Originally the outer and inner openings lie near together; later they move so far apart that the outer opening of the canal is united with the hindgut." (Hertwig.)

f. Summary of Early Development.

If the student has observed carefully the character of the developmental changes he has noted three phases of development going on at the same time: (I) The tendency to *unequal growth,* manifested at particular places and occurring at particular times, resulting in the general morphologic unfolding; (II) the histologic differentiation manifesting itself in the development of new tissues (histogenesis); (III) the physiologic division of labor, manifested by the general division of the functions into those of *external relations* and those of *internal relations;* and by the beginning development of various systems of organs—nervous system, circulatory system, excretory system, etc.

(*a*) THE PRINCIPLE OF UNEQUAL GROWTH is manifested in the chick during its first two days of development by: (I) the *invagination* of the blastopore; (II) the *evagination* of the medullary folds; (III) the evagination of the three primary brain vesicles from the anterior end of the neural tube; (IV) the subsequent evagination of the optic vesicles from the forebrain vesicle; (V) the evagination of the lateral folds of mesoblast from the median hypoblast; (VI) the *separation* of the muscle plates and their subsequent segmentation; (VII) the general emigration, from the mesoblast, of the elements of the mesenchyme; (VIII) the invagination of the pronephric canals.

(*β*) THE PRINCIPLE OF HISTOLOGIC DIFFERENTIATION is manifested in histogenesis:

- **HISTOGENESIS.** Origin of Tissues.
  - **I. ECTODERMIC TISSUES.** Tissues of external relation.
    - **EPIBLAST PROPER.**
      - *Cuticle and appendages*, *e.g.*, hair, nails, sebaceous and sweat glands, enamel of teeth.
      - Epithelium of conjunctiva and cornea.
      - " nasal tract with glands.
      - " mouth with glands.
      - " anus and lower rectum.
      - " auditory canal.
    - **NERVOUS SYSTEM.** Neuroblast.
      - *Central nervous system*, *i. e.*, brain and cranial nerves, spinal cord, and spinal nerves.
      - *Sensory apparatus.*
        - Retina, cryst. lens, taste buds, auditory nerves, olfactory nerves, tactile bodies.
  - **II. ENTODERMIC TISSUES.** Tissues of internal relation.
    - **MESOBLAST.**
      - *Primitive segments.*
        - Voluntary muscular system.
      - *Somatic Mesothelium.*
        - Somatic pleura and
        - " peritoneum.
        - Epithelium of genito-urinary tract.
      - *Splanchnic Mesothelium*
        - Lung.-pleura, pericardium.
        - Splanchnic peritoneum.
      - *Mesenchyme.*
        - CONNECTIVE TISSUES: Bone-cartilage, ligament, dentine, areolar tissue, tendon.
        - INVOLUNTARY MUSCULAR SYSTEM.
        - VASCULAR ENDOTHELIUM, BLOOD, AND SPLEEN.
    - **HYPOBLAST.**
      - Epithelium of *digestive tract* (exclusive of mouth and anus). Inclusive of liver, pancreas.
      - Epithelium of *respiratory tract*.
      - " urinary *bladder* and *urethra*.
      - " Eustacian tube and tympanum.
      - " tonsils.
      - " thymus body.
      - " thyroid body.
    - **NOTOCHORD.**

6. THE FETUS: ORGANOGENESIS.

The terms *fetus* and *embryo* are used synonymously by some authors, while by others they are given different significations. Gould defines fetus as "the embryo in later stages of development," but uses embryo and fetus synonymously. The author, following in a general way the *American Text-book of Obstetrics*, will use the terms in the following sense: the *embryo* is the young in its early stages of development *when tissues are being developed;* the *fetus* is the young at a later stage of development *when organs, especially systems of organs, are being given their finishing touches*—*i. e.*, the term embryo covers the period of histogenesis, and the term fetus covers the period of organogenesis.

Under the caption *fetus* we shall briefly discuss the development of the various systems of organs.

a. The Circulatory System.

1. **General Considerations.**—(α) THE SIMPLEST HEART among the vertebrates is a rhythmically contracting tube: the heart of the highest vertebrate is at first a rhythmically contracting tube.

(β) INTERMEDIATE CLASSES OF VERTEBRATES have *two-* and *three-*chambered hearts, and the highest classes have the four-chambered heart: the heart of the highest vertebrate passes from the original tubular condition through the two- and three-chambered condition during fetal development and finally after birth assumes the functionally four-chambered heart.

FIG. 317

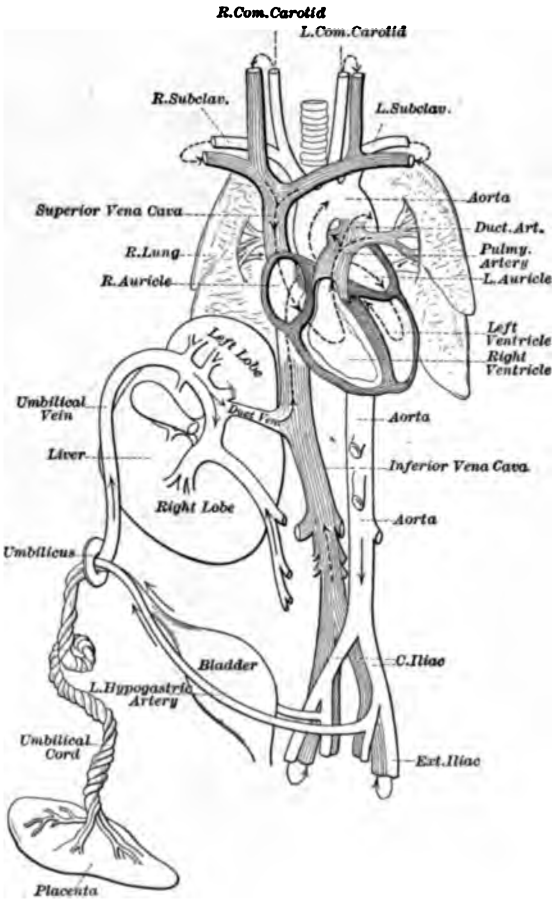
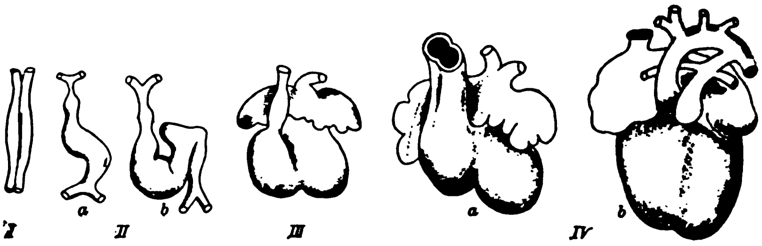


Diagram of the fetal circulation. (Kirke.)

(γ) The One- and Two-chambered Condition of the Heart makes it necessary for the heart contractions to propel the blood in one circuit through a double system of capillaries: (i) the capillaries of the respiratory system, and (ii) the capillaries of the general circulation. The circulatory system of the highest vertebrates passes through this condition and reaches, in extrauterine life, a condition in which one-half of the heart propels the blood through the respiratory system while the other half propels it through the general system.

	CHANGE DURING PERIOD.	CONDITION AT END OF PERIOD.	
I.	....	Straight muscular tube.	I
II.	**Curve** of Heart-tube, through increase in length of Heart and no increase in length of pericardium.	Heart in S-shaped curve, with venous end in left dorsal region and arterial end in right ventral region.	II.
III.	**Dilatation** laterally of venous end and general **Dilatation** of central or ventracular segment and **Dilatation** of Bulbus Arteriosus.	Heart of Two Chambers, one double-lobed, single-chamber auricle dorsally and a single-chambered ventricle ventrally	III.
IV.	**Division** of whole Heart: 1st. Auricle into left and right. 2d. Ventricle into left and right. 3d. Bulbus Arteriosus into Aorta and Pulmonary Artery.	Heart of Four Chambers. Left Auricle, Left Ventricle and Aorta continuous and Right Auricle, Right Ventricle and Pulm. Art. continuous.	IV.

Fig. 318



Development of the heart. The four principal stages are shown at *I* to *IV*; *a* and *b* are two phases of the same stage. (Hertwig.)

(δ) In the Lower Vertebrates the blood passes from the heart directly into a system of branchial arches or gill-arches; the highest vertebrate possesses this system of gall-arches during the early part of its development. These arches are gradually reduced during the three- and four-chambered stages. Our aortic and pulmonary arches represent the last two pairs of arches.

(ε) In the Amphibia and Reptiles, classes of vertebrates which possess three-chambered hearts, the purer blood passes to the anterior part of the body, while the less pure blood passes to the posterior part of the body. In the human fetus the functionally three-chambered heart distributes the blood in a similar way. This probably accounts, in part, for the large head and small legs of the fetus (Fig. 317).

2. **Special Metamorphosis of the Heart.**—During the second day of the chick's development the heart is practically a straight tube formed by the fusion, along the median line, of a double, tubular heart fundament, continuous posteriorly with the two omphalomesaraic veins and anteriorly with the bifurcated aorta. The endothelial partition of the heart soon disappears, leaving a single tube with somewhat thickened muscular walls. The dorsal aortæ, in the mean time, pass laterally around the alimentary canal and fuse ventrally, forming the single aortic trunk which joins the anterior end of the heart, or bulbus arteriosus. As soon as the posterior venous junctions and the anterior arterial junction has been effected the already slowly and irregularly beating heart begins to send the elements of the blood through the system of tubes, the direction of the stream being at first determined not by valves, but by virtue of a posteroanterior peristalsis.

FIG. 319

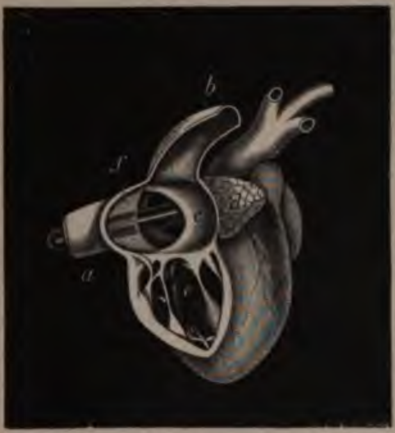


FIG. 320

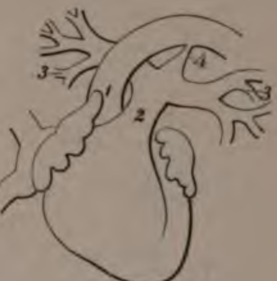


FIG. 319.—Heart of the human fetus, at the end of the sixth month: *a*, inferior vena cava; *b*, superior vena cava; *c*, cavity of the right auricle, laid open from the front; *d*, appendix auricularis; *e*, cavity of the right ventricle; *f*, Eustachian valve. The bougie, placed in the inferior vena cava, can be seen passing behind the Eustachian valve, just below the point *f*, then crossing, behind the right auricle, through the foramen ovale to the left side of the heart. (Dalton.)

FIG. 320.—Heart of infant, showing disappearance of the artificial duct after birth. 1, aorta; 2, pulmonary artery; 3, 3, pulmonary branches; 4, ductus arteriosus becoming obliterated. (Dalton.)

During the subsequent few hours the pulsations become regular and rapid, and the development of valves accompanies the gradual metamorphosis of the heart. The metamorphosis of the heart may be considered in four principal changes (Figs. 318, 319, and 320).

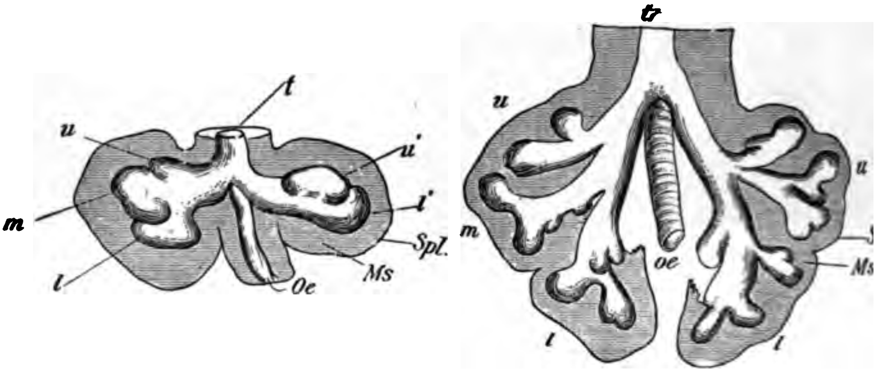
b. The Respiratory System.

1. **General Considerations.**—(*α*) THE SIMPLEST VERTEBRATE respiratory system is composed of a series of gill-arches: *The highest vertebrate has gill-arches in early embryonic life.*

(*β*) IN THE HIGHEST FISHES there is a combination of gills and swim-bladder, which is a saccate evagination or outgrowth of the alimentary tract: *In amphibia* the gills are usually secondary in importance to the saccate lungs, which are homologous to the swim-bladder: *In the highest vertebrate* the gills are rudimentary structures confined to embryonic life, and never functional while the function of respiration is performed during the whole period of extrauterine life by the lungs.

2. **Special. The Development of the Lungs.**—At the beginning of the third day in the chick, on the tenth day in the rabbit, and in the human embryo when it reaches a length of about 4 mm., there arises on the ventral side of the œsophagus a groove which is slightly enlarged at its anterior end. Soon the groove-like evagination becomes separated from the alimentary tube by two lateral ridges; this is the first indication of a differentiation into œsophagus and trachea. There then grow out from the enlarged posterior ends of the groove two small sacs toward the two sides of the body—the fundaments of the right and left lung.

FIG. 821



A B

Early development of the lung: *t*, trachea; *Oe*, œsophagus; *u*, *m*, *l*, upper middle and lower right lobes; *u'*, *l'*, upper and lower left lobes; *Spl.*, splanchnopleure; *Ms.*, mesenchyme. (From Hertwig, after His.)

These lung sacs are enveloped in a thick layer of mesenchymic connective tissue which is covered externally by the thin splanchnic mesothelium—the future lung-pleura. Two stages are recognizable in the metamorphosis of the primitive lung sacs of man and of mammals.

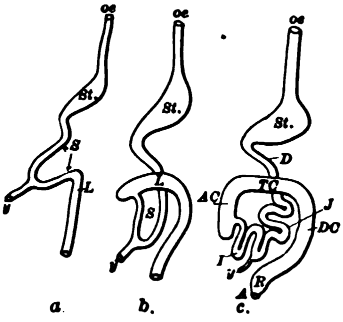
(I) *The first bud-like outgrowths on the two sides of the body are not symmetric* because the left *lung sac produces two* and the right *lung sac produces three bud-like enlargements* (Hertwig). These buds are the fundaments of the lobes of the lungs. From this point on the division is dichotomous. Continuous division and evagination proceed during six months in the human embryo. During this period the terminal branches are simply saccate or vesicular, and are called *primitive lung vesicles* (Fig. 321, *B*).

(II) During the last three months of intrauterine life "there arise close together on the fine terminal of the bronchial tree—on the alveolar passages and on their terminal vesicular enlargements—very numerous small evaginations—the *pulmonary alveoli*" (Kölliker). These are only one-third to one-fourth as large in the fetus as in the adult, and the extrauterine growth of the lung is to be attributed to their expansion rather than to their multiplication.

c. The Digestive System.

1. **General.**—(*α*) In All Vertebrates the stomach is produced by a simple dilatation of the alimentary canal, just behind the heart in the lower vertebrates and just posterior to the diaphragm in mammalia (Fig. 322).

Fig. 322



Development of the alimentary canal: *oe*, œsophagus; *St*, stomach; *S*, small intestine; *L*, large intestine; *y*, yolk duct; *D*, duodenum; *J*, jejunum; *I*, ileum; *AC*, *TC*, *DC*, ascending, transverse, and descending colon; *R*, rectum; *A*, anus.

(*β*) In All Vertebrates two glands are evaginated from the duodenum—the *liver* is evaginated into the ventral mesentery and *pancreas* into the dorsal.

2. **Special Development of Digestive Glands.**—(*α*) The Liver early becomes bilobed—later these two primitive lobes are variously subdivided in different classes of vertebrates—and the evaginations take the form of thick-walled tubes or "*hepatic cylinders*" which unite into a network. The small lumina of the cylinders become the bile-ducts, which are surrounded by the secreting parenchyma of the liver. This latter, as well as the epithelial lining of all gall-ducts, is of hypoblastic origin, while the connective-tissue framework and the vascular system of the liver are from the mesenchyme, the organ being encapsuled with splanchnic peritoneum.

(*β*) The Pancreas follows a general course of development quite parallel to that of the liver.

d. The Urogenital System.

For general considerations see above under "Origin of the Urinary System."

FIG. 323

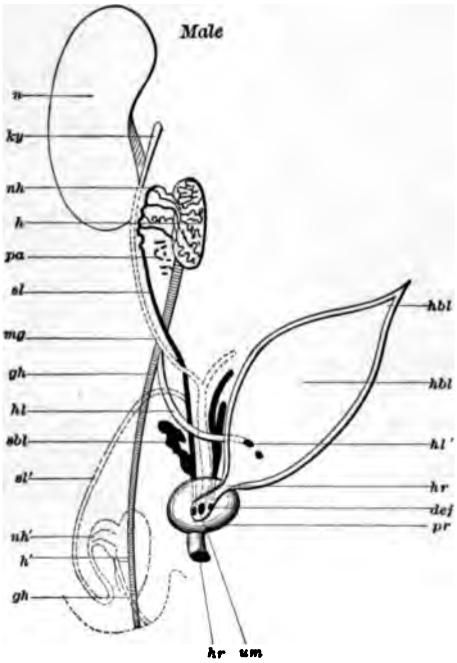


Diagram to illustrate the development of the male sexual organs of a mammal from the indifferent fundament of the urogenital system. The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the male sexual organs take after the completion of the descensus testiculorum. *n*, kidney; *h*, testis; *nh*, epididymis; *pa*, paradidymis; *hy*, hydatid of the epididymis; *sl*, vas deferens; *mg*, degenerated Müllerian duct; *um*, uterus masculinus, remnant of the Müllerian ducts; *gh*, gubernaculum Hunteri; *hl*, ureter; *hl'*, its opening into the bladder; *sbl*, vesiculæ seminales; *hbl*, urinary bladder; *hbl'*, its upper tip, which is continuous with the ligamentum vesicoumbilicale medium (urachus); *hr*, urethra; *pr*, prostata; *dej*, external orifice of the ductus ejaculatorii. The letters *nh'*, *h'*, *sl'*, indicate the position of the sexual organs after the descent has taken place. (Hertwig.)

FIG. 324

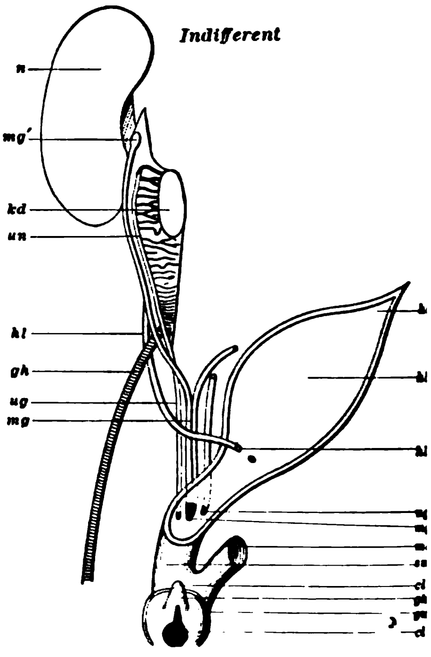


Diagram of the indifferent fundament of the urog
tal system of a mammal at an early stage. n, kidn
kd, sexual gland; *un*, primitive kidney; *ug*, mesonep
duct; *mg*, Müllerian duct; *mg'*, its anterior end;
gubernaculum Hunteri (mesonephric inguinal l
ment); *hl*, ureter; *hl'*, its opening into the urinary b
der; *ug''*, *mg''*, openings of the mesonephric and
lerian ducts into the sinus urogenitalis (*sug*); *md*,
tum; *cl*, cloaca; *ghö*, sexual eminence; *gw*, se
ridges; *cl'*, external orifice of the cloaca; *hbl*, uri
bladder; *hbl'*, its elongation into the urachus (the fu
lig. vesicoumbilicale). (Hertwig.)

1. **The Indifferent Stage.**—This stage is characterized by all the organs being contained in two longitudinal urogenital ridges, one on each side of the body and projecting from the dorsal wall into

the peritoneal cavity. At the caudal end of the abdomen the two ridges draw closer together and finally come into contact with the anal region of the alimentary canal. The substance of the ridge comprises the Wolffian body of mesonephros and the genital epithelium. The ducts are two in number and are supposed to be the result of longitudinal division of the original pronephric duct. The inner one of the two resulting ducts is the mesonephric or Wolffian duct, and during the period when the mesonephros functions as a urine-excreting organ conducts the urine to the cloaca; this condition is permanent in fishes and amphibians. The outer one of the resulting ducts is the Müllerian duct. Now, in the male *the Wolffian duct* becomes the *genital duct*, while *in the female the Müllerian duct becomes the genital duct.*

FIG. 325

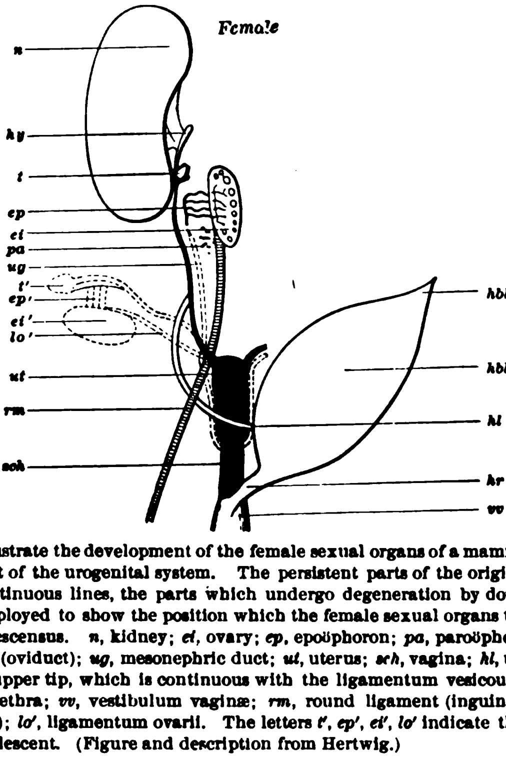


Diagram to illustrate the development of the female sexual organs of a mammal from the indifferent fundament of the urogenital system. The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the female sexual organs take after the completion of the descensus. *n*, kidney; *ei*, ovary; *ep*, epoöphoron; *pa*, paroöphoron; *hy*, hydatid; *t*, Fallopian tube (oviduct); *ug*, mesonephric duct; *ut*, uterus; *sch*, vagina; *hl*, ureter; *hbl*, urinary bladder; *hbl'* its upper tip, which is continuous with the ligamentum vesicoumbilicale medium (urachus); *hr*. urethra; *vv*, vestibulum vaginæ; *rm*, round ligament (inguinal ligament of the primitive kidney); *lo'*, ligamentum ovarii. The letters *t'*, *ep'*, *ei'*, *lo'* indicate the positions of the organs after the descent. (Figure and description from Hertwig.)

2. **The Differentiated Stage.**—(*a*) CHANGES COMMON TO BOTH SEXES are: (I) The union of the caudal ends of the urogenital ridges to form a *single median* UROGENITAL CORD. (II) The ducts of the *urogenital cord* open into a cloaca with the rectum. (III) The

cloaca gradually divides into the urogenital sinus and the anus. (iv) The allantois also opens into the cloaca and in extrauterine life *the dilated remnant* of the *allantois becomes* the *urinary bladder.* (v) *From the lower end* of the *mesonephric* or *Wolffian duct there evaginates* the metanephric duct or *ureter.* This grows into that part of the *urogenital ridge* which lies just posterior to the Wolffian body or mesonephros. The mass of the urogenital ridge now lying about the dilated and divided ureter is the fundament of the metanephros or permanent kidney. While the fundament with the ureter gradually advances anteriorly, the end of the ureter differentiates into the pelvis, calyces, and the collecting tubules of the pyramidal portion, and the cortical fundament gradually develops the Malpighian corpuscles and the convoluted tubules. (vi) The genital epithelium in the region of the mesonephros develops into the *genital gland,* while the Wolffian body—mesonephros—lapses into functional or rudimentary appendages of that gland.

(β) Sexual Differentiation. (Hertwig.) (See Figs. 323–325.)

Male Sexual Parts.	Indifferent: common form from which both arise.	Female Sexual Parts.
Testis. Seminal ampullæ and tube.	Germical epithelium.	Ovary. (Ovarian follicles.)
a. Epididymis. b. Paradidymis.	Mesonephros or Wolffian body.	a. Epoöphoron. b. Paroöphoron (Parovarian or organ of Rosemüller).
Vas Deferens and Seminal Vesicles.	Mesonepheric duct.	
Hydatid of epididymis. Sinus prostaticus (uter. masc.)	Müllerian duct.	Uterus and vagina. Oviduct and fimbriæ.
Kidney.	Metanephros.	Kidney.
Ureter.	Metanephric duct.	Ureter.
Gubernaculum Hunteri.	*Inguinal ligt. of Mesoneph.*	*Round ligament.*
Urethra, membranous and Prostatic part.	Sinus urogenitalis.	Vestibulum vaginæ.

e. The Central Nervous System.

1. **General Considerations.**—(*α*) In all vertebrates the central nervous system is developed out of the thickened region of the outer germ layer which is designated as the *medullary plate.* The medullary plate is folded together to form the *neural tube.*

(β) In the lowest vertebrates the neural tube is not differentiated into *brain* and *spinal cord.* In the higher vertebrates there is at first no differentiation between brain and spinal cord.

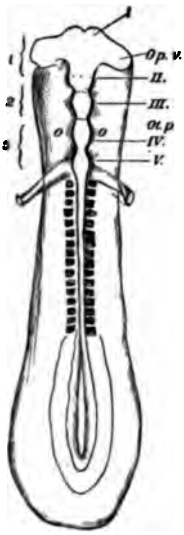
(γ) In fishes the brain consists of five lobes not very unlike in size. An early step in the development of the brain of higher vertebrates is the formation of five lobes or vesicles.

(δ) The ascending scale of vertebrates is marked by an *increasing preponderance* of the *cerebrum over* the *other segments* of the brain. THE HIGHEST VERTEBRATE in its embryonic development shows an ever-increasing preponderance of the cerebrum over other parts.

2. **Special. Development and Metamorphoses of the Human Brain.**—(*a*) The part of the neural tube which forms the brain becomes segmented into the three PRIMARY BRAIN VESICLES mentioned above.

(β) The lateral walls of the forebrain vesicles are evaginated to form the *Optic Vesicles*, and the anterior wall to form the *secondary Forebrain Vesicle*, CEREBRUM, or Prosencephalon.

FIG. 326



(γ) The hindbrain vesicle is divided by constriction into the vesicle of the CEREBELLUM—Metencephalon—and the MEDULLA—Myelencephalon.

(δ) Thus, from the three primary brain vesicles there arise five SECONDARY VESICLES arranged in a single series, one after the other in a straight line (Fig. 326).

(I) *Cerebrum*—prosencephalon.

FIG. 327

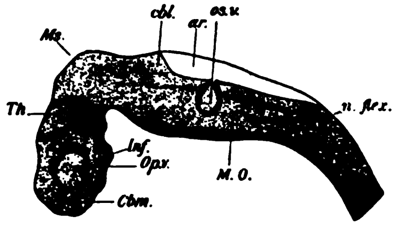


FIG. 326.—Primitive brain and spinal cord of man: 1, 2, 3, the three primary brain vesicles (forebrain, midbrain, and hindbrain). *I.*, prosencephalon; *Op.v.*, optic vesicle; *II.*, thalamencephalon; *III.*, mesencephalon; *Ot.p*, aural pits; *IV.*, metencephalon; *V.*, myelencephalon. (After Haekel.)

FIG. 327.—A somewhat later stage of the human brain: *Cbm.*, cerebrum (prosencephalon); *Inf.*, infundibulum; *Th.*, interbrain (thalamencephalon); *Ms.*, midbrain (mesencephalon); *cbl.*, cerebellum (metencephalon); *ar.*, area rhomboidalis; *M.O.*, medulla oblongata (myelencephalon); *n. flex.*, nuchal flexure. (After His.)

(II) *Interbrain*—thalamencephalon—with the laterally attached optic vesicles.

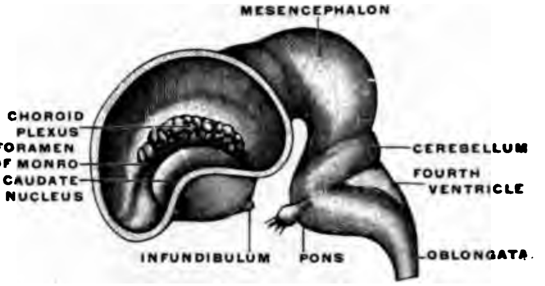
(III) *Midbrain*—mesencephalon.

(IV) *Cerebellum*—metencephalon.

(V) *Medulla oblongata*—myelencephalon.

(ε) The originally straight axis uniting the brain vesicles to one another later becomes, at certain places, sharply bent: (I) The *Nuchal Flexure* is a ventral bending of the medulla, forming the *nuchal protuberance dorsally*. (II) The *Pontal Flexure* is a dorsal bending in the region of the pons Varolii. (iii) The *Cephalic Flexure* is a marked and persistent ventral bending of the midbrain, resulting in the *cephalic protuberance*. The nuchal and the cephalic protuberances are obscured by subsequent development (Fig. 328).

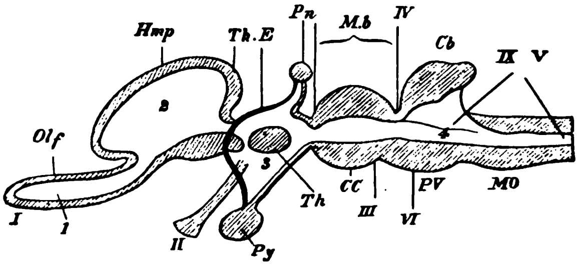
FIG. 328



Lateral view of the brain of a calf embryo of five cm. The outer wall of the hemisphere is removed so as to give a view of the interior of the left lateral ventricle. (From Hertwig.)

(ζ) In the metamorphosis of the vesicles the following processes take place: (i) certain regions of the walls become thickened, other regions become thinner and do not develop nervous substance (roof membranes of third and fourth ventricles); (ii) the walls of the vesicles may be evaginated or invaginated; (iii) some of the vesicles greatly exceed in their growth the remaining ones (cerebrum, cerebellum) (Fig. 328).

FIG. 329



Longitudinal and vertical diagrammatic section of a vertebrate brain. Lamina terminalis is represented by the strong black line joining *Pn* and *Py*. *Olf*, olfactory lobes or rhinencephalon; *Hmp*, cerebral hemispheres, mantle or prosencephalon; 3 with *II*, *Py*, and *Pn*, thalamencephalon or interbrain; *M.b*, *III*, midbrain or mesencephalon; *Cb*, *PV*, metencephalon; 4, fourth ventricle; *MO*, medulla. (Huxley.)

The four ventricles of the brain and the aqueduct of Sylvius are derived from the cavities of the vesicles.

Of the five vesicles the midbrain undergoes the least metamorphosis.

The cerebral vesicle is divided by the development of the *longitudinal fissure* and the *falx cerebri* into lateral halves, the *cerebral hemispheres.*

In man the cerebral hemispheres finally exceed in volume all the remaining parts of the brain and grow out in every direction, forming a "cerebral mantle" over the other segments of the brain.

THE DEVELOPMENT OF THE BRAIN (HERTWIG). (See Fig. 329.)

(f) floor: (r) roof; (w) Walls.

				CAVITY.
The development of the brain	Primary forebrain vesicle	I. Forebrain CEREBRUM Prosencephalon	Olfactory lobes (f) Cerebral cortex (r and w) Ant. perf. lamina (f) Corpus striatum (f) Corpus callosum (r and w)	Lateral ventricles (1st and 2d).
		II. INTERBRAIN Optic thalamus Thalamencephalon	Optic chiasm (f) Roof-memb. of third vent. (r) Optic thalami (w) Tuber cinereum with infundibulum (f) Corpora albicantia (f) Pineal gland (r)	Third ventricle.
	Midbrain vesicle	III. MIDBRAIN Corpora quadrigemina Mesencephalon	Post. perf. lamina (f) Peduncles of cerebrum (f) Corpora quadrigemina (r) Laqueus (w)	The aqueduct of Sylvius.
	Primary Hindbrain vesicle	IV. Hindbrain CEREBELLUM Metencephalon	Pons Varolii (f) Cerebellar cortex (r and w) Crura cerebelli ad pontem (w)	Fourth ventricle.
		V. Afterbrain MEDULLA OBL. Myelencephalon	Medulla oblongata (f) Roof-memb. of 4th ventricle (r) Peduncles of cerebellum (w)	Fourth ventricle.

7. THE FETAL ENVELOPES.

a. The Fetal Membranes.

The term fetal membranes may be used for that portion of the fetal envelopes developed from the ovum. A part of the fetal envelopes is produced by the maternal organism. If one refers to Fig. 311, *af,* he will find a crescentic dark field which represents a transverse ridge of epiblast anterior to the embryo near the anterior margin of the blastoderm. As soon as the mesoblast is formed, and divided into somatopleure and splanchnopleure, the former takes part in the formation of this fold, while the latter with the hypoblast remains in close contact with the yolk. By the time that the primitive segments begin to appear the amniotic fold has taken on a horseshoe shape enclosing the head end of the embryo and sending two ridges toward the caudal end of the embryo. A cross-section of the embryo at this stage will appear something like Fig. 330. The two lateral folds approach each other over the median dorsal line of the embryo and meet and fuse from before backward, thus forming a double sac, an inner true AMNION, composed of epiblast internally and mesothelium externally; and an outer false amnion or CHORION, composed of epiblast externally and mesothelium internally. (See Fig. 331.) The chorion presents villi over a considerable portion of the surface of the ovum. At first these villi are practically equal in development, but after the allantois becomes developed the villi in the region of that organ are rapidly increased in size, while those in other regions become obliterated. These facts are represented in Fig. 332.

The ALLANTOIS is an evagination from the ventral side of the primitive hind gut and is composed of hypoblast internally and mesothelium externally. While the yolk sack (*ds*) decreases in size the allantois (*al*, Fig. 332) increases; finally reaching the chorion, where it forms the fetal portion of the placenta. The allantois is accompanied by two umbilical arteries and an umbilical vein. These send branches into the chorionic villi of the placenta.

FIG. 330

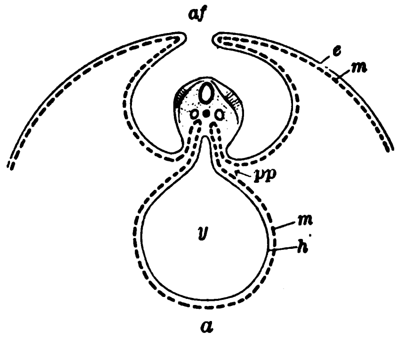
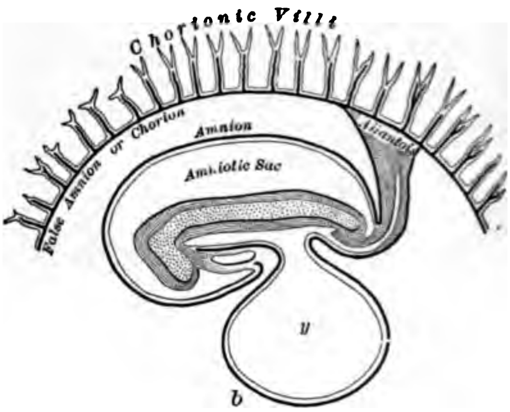


FIG. 331



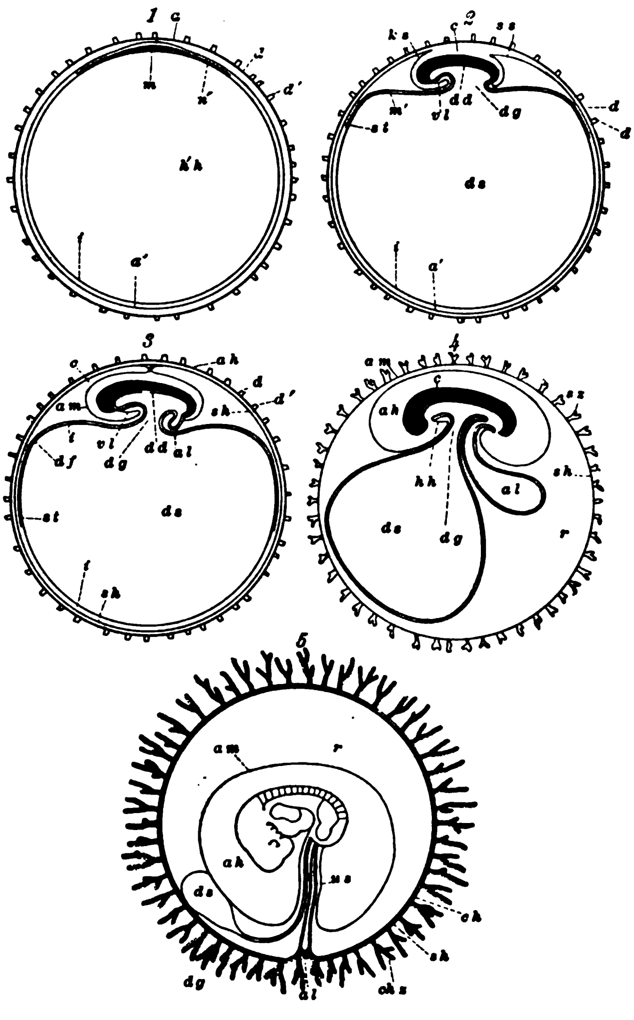
Diagrammatic figures of the development of the fetal membranes: *af*, amniotic fold; *e*, epiblast; *m*, mesoblast; *h*, hypoblast; *pp*, pleuroperitoneal cavity. Note that the amniotic sac is lined with epiblast, and that the chorion is lined with somatopleure, the epiblast being external and covering the chorionic villi.

The UMBILICAL CORD is composed of the arteries and vein, the shriveled yolk stalk, the allantoic stalk, a gelatinous embryonic connective tissue, and, in early stages, the whole enclosed in amnion. A careful study of Figs. 331 and 332 will reveal the relations of these structures much more clearly than a description could do.

b. Maternal Portion of Envelopes: Deciduæ and Placenta.

The maternal organism plays an important part in the formation of the fetal envelopes. Figs. 333, 334 and 335 show the formation of the deciduæ. Fig. 336 shows the three portions of the deciduæ: (I) *Decidua vera* lining the body of the uterus; (II) *Decidua reflexa*,

FIG. 332



Diagrammatic figures, illustrating the development of the mammalian embryo and the fetal membranes: 1, the blastodermic vesicle invested in the zona pellucida, and showing at its upper pole the embryonic area; 2, shows the pinching off of the embryo from the yolk sac and the formation of the amnion; 3, further development of amnion and commencement of allantois; 4, completion of amnion and growth of allantois. The false amnion, or subgonal membrane, gives off villous process. 5, the allantois has grown all around the vesicle, and gives off processes into the villi which are much larger than before. The yolk sac is greatly reduced in size. *a*, epiblast of embryo; *a'*, epiblast of non-embryonic part of blastodermic vesicle; *al*, allantois; *am*, amnion; *ch*, chorion; *ch* 2, chorionic villi; *d*, zona pellucida; *d'*, processes of zona; *dd*, embryonic hypoblast; *df*, area vasculosa; *dg*, yolk stalk; *ds*, yolk sac; *e*, embryo; *hh*, pericardial cavity; *i*, non-embryonic hypoblast; *kh*, cavity of blastodermic vesicle; *ks*, head fold of amnion; *m*, embryonic mesoblast; *n*, non-embryonic mesoblast; *r*, space between true and false amnion; *sh*, false amnion, or subgonal membranes; *ss*, veil fold of amnion; *st*, sinus terminalis; *st*, processes of zona pellucida; *vl*, ventral body wall of embryo. (Kölliker.)

reflected over the egg; (III) *Decidua serotina*, where the chorionic villi are developed. The relation of the maternal to the fetal membranes is shown in Fig. 335. Fig. 336 shows similar structures somewhat less diagrammatic.

FIG. 333

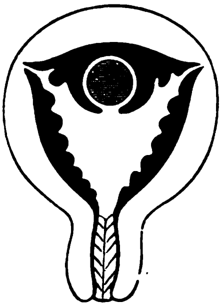


FIG 334

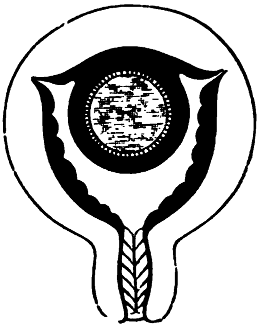
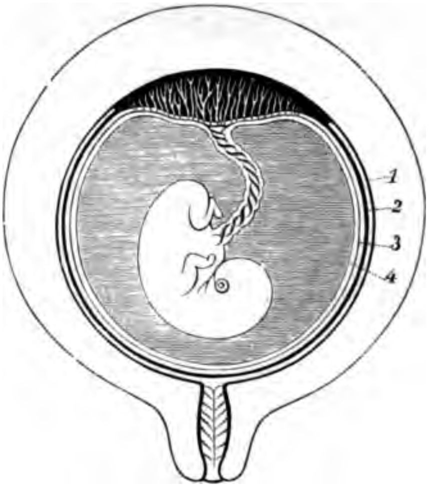


FIG. 333.—Impregnated uterus, with folds of decidua growing up around the egg. The narrow opening, where the folds approach each other, is seen over the most prominent portion of the egg. (Dalton.)

FIG. 334.—Pregnant uterus, showing the formation of the placenta by the local development of the decidua and the chorion. (Dalton.)

FIG. 335



Pregnant human uterus and its contents, about the end of the seventh month, showing the relations of the cord, placenta, and membranes: 1, decidua vera; 2, decidua reflexa; 3, chorion; 4, amnion. (Dalton.)

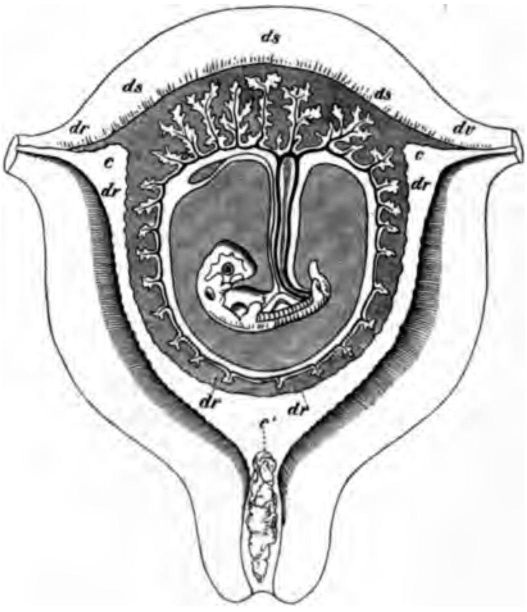
The placenta is composed of the serotine decidua with its large venous sinuses through which the maternal blood circulates; of the chorion and amnion with the fetal arteries and vein. In the placenta the maternal and fetal blood come into relation. There are three tissue layers between the fetal and maternal blood. The epiblast and mesothelium of the villus and the endothelium of the capillaries. Through these fissures the fœtus receives nourishment from the maternal organism.

8. THE PHYSIOLOGY OF THE EMBRYO AND FETUS.

a. Nutrition.

1. **Foods, Digestion, and Absorption.**—The origin of the animal individual from an ovum is practically universal (protozoa excepted, perhaps). The fertilized ovum consists of the minute segmentation nucleus and the yolk mass which represents the first installment of maternal nourishment. The yolk mass is relatively large in birds and reptiles, and relatively small in mammals.

FIG. 336



Diagrammatic view of a vertical transverse section of the uterus at the seventh or eighth week of pregnancy: *c*, *c*, *c'*, cavity of uterus, which becomes the cavity of the decidua, opening at *c*, *c*, the cornua, into the Fallopian tubes, and at *c'* into the cavity of the cervix, which is closed by a plug of mucus; *dv*, decidua vera; *dr*, decidua reflexa, with the sparser villi embedded in its substance; *ds*, decidua serotina, involving the more developed chorionic villi of the commencing placenta The fetus is seen lying in the amniotic sac; passing up from the umbilicus is seen the umbilical cord and its vessels passing to their distribution in the villi of the chorion; also the pedicle of the yolk sack, which lies in the cavity between the amnion and chorion. (Allen Thomson.)

(*a*) **Birds** may be taken as an example of those animals whose embryos are provided with a large yolk mass. The hen's egg weighs 50 gms., of which 5 gms. is shell and 45 gms. food. The WHITE weighs 30 gms. and consists of *proteins* (albumins and globulins) 3 gms., *fats* 0.3 gm., *salts* 0.1 gm., *water* 26.6 gms. The YOLK weighs 15 gms. and consists of *proteins*, 1.7 gms., *fat* 3 gms., *vitelline*, *nuclein*, *glycogen* 0.2 gm., *lecithin* 1 gm., *salts* 0.1 gm., *water* 9 gms. The salts contain bone-making material—phosphates and carbonates; also blood and tissue constituents—chlorides, phosphates, and carbonates.

The chicken from a 50-gm. egg weighs 35 gms., 10 gms. having been lost in katabolism, and passed through the pores of the shell as CO_2 and H_2O. The small amount of nitrogenous excreta remains within the shell, generally within the cloaca of the chick, to be voided soon after it leaves the shell. The chicken is 80 per cent. water (28 gms. water and 7 gms. solids), while the egg is 79.1 per cent. water.

(*b*) **Mammals** present a more complex problem. The mammalian ovum has a small proportion of yolk and is retained within the uterus of the mother long after this meagre supply is exhausted. After the yolk mass is exhausted the embryo "takes root" in the maternal tissues and draws plasma and oxygen from the mother. The mammalian mother furnishes her intrauterine offspring with two sources of food—the *yolk mass* and her own *blood*. Besides this there is a special provision for the extrauterine period when the young mamma is more or less helpless, viz., the *milk* which the mother secretes.

α THE YOLK MASS probably has about the same chemical composition in the mammal as in the bird. This yolk mass must be *digested*. It is surrounded by the hypoblast which is to furnish the epithelium of the alimentary tract. There are no glands to secrete a digestive fluid at the period when the yolk is consumed, yet the yolk can be absorbed only after solution. The hypoblastic cells lining the yolk sac and cœlenteron must digest and absorb the yolk mass. In this connection it must not be forgotten that the white of the bird's egg is outside of the epiblast of the chorion and must be absorbed by the chorion. In the mammal the epiblast of the chorion is the principal absorbing surface.

β THE MATERNAL BLOOD is the source from which the mammalian fetus draws sustenance. The special organs involved in this process have been mentioned above. Maternal red corpuscles do not pass into the fetus. Maternal white corpuscles probably do pass from maternal to fetal circulation. It is easy to see how all soluble salts can readily pass from maternal to fetal plasma, and the effect of various drugs upon the fetus when given to the mother demonstrates that they do pass from one to the other. Just how plasma proteins pass from the mother to the fetus is a puzzle still unsolved. Some have suggested that the maternal plasma proteins are peptonized, diffuse through the dividing membranes, and are changed back to protein; others think the white corpuscles carry protein from mother to young.

Toward the end of intrauterine life the mammalian fetus swallows a portion of the amniotic fluid. The amount of amniotic fluid is very small at first, but increases progressively with the period of gestation. This fluid diffuses or filters into the amniotic sac from the maternal and, perhaps, fetal lymph spaces. It contains water (an important constituent of embryonic tissue) and various salts with small portions of other foodstuffs.

2. **Circulation.**—(α) THE CIRCULATION OF THE EMBRYO is the *vitelline circulation* or the system of vessels which spread over the yolk, beginning with the area vasculosa. The principal arteries are the paired vitelline arteries which pass out on either side, branching profusely as far as the vena terminalis. From the vena terminalis or terminal sinus a system of venules and veins brings the blood back to the venous sinus, from which it passes into the heart.

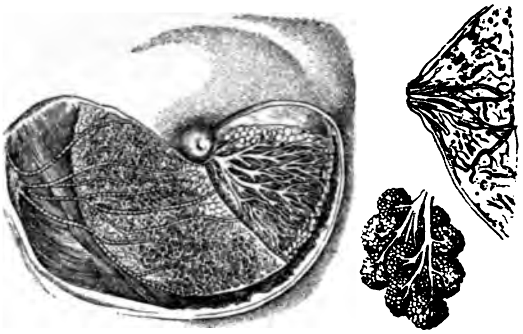
(β) THE CIRCULATION OF THE FETUS, "*Fetal Circulation,*" a diagram of which appears on page 753, is a special adaptation of the permanent circulation. The permanent circulation sends the blood to the lungs for oxidation of the hæmoglobin, but, the fetal lungs not being functional, there is a means provided to direct the blood stream from them. This necessitates two important structures peculiar to the fetus: (I) the *foramen ovale,* through interauricular septum; (II) the *ductus arteriosus,* from the pulmonary artery to the arch of the aorta. Other peculiarities of the fetal circulation are: (III) the *hypogastric arteries,* which carry impure blood from the iliac arteries to the umbilical arteries, through which it passes to the placenta for oxidation of the hæmoglobin; (IV) the *ductus venosus,* from the umbilical vein to the vena cava, which provides for the direct passage of a large portion of the pure blood to the left side of the heart through the foramen ovale. The four structural peculiarities of the fetal circulation lead to the following functional peculiarities: (I) the circulation of venous blood in the hypogastric and umbilical arteries; (II) of arterial blood in the umbilical vein and ductus venosus; (III) of arterial blood in the ascending vena cava, mixed, however, with venous blood from the lower extremities; (IV) of the mixed blood (the purest which enters the heart) in the arteries of the head and anterior extremities; (V) of the least pure blood—further mixed with the blood from the ductus arteriosus—to the posterior extremities and the placenta.

3. **Respiration.**—In birds and reptiles the respiration takes place readily through the porous shell and shell membrane, the vitelline arteries bringing the impure blood from the body of the embryo out upon the surface of the yolk. If the shell be varnished the chick will smother.

In mammals the respiration is carried on through the placenta. The blood of the fetus is brought into relation with the maternal blood. The oxygen pressure in the fetal blood is much lower than that in the maternal blood, so that the oxygen passes readily from maternal to the fetal blood through the dividing membranes.

4. **Metabolism and Excretion.**—In the parasitic life led by the embryo and fetus the anabolic processes are greatly in excess of the katabolic processes. The food is presented to the fetus so nearly ready for assimilation that almost no energy is consumed in preparation of the food. This food must be transported, however, and this transportation by the circulatory system involves the liberation of kinetic energy of mechanical motion. This energy can be liberated only through katabolism of embryonic tissues and fluids. The katabolites are for the most part CO_2 and H_2O, but some nitrogenous compounds (urea, etc.) are formed, and these must be thrown out of the body of the embryo. At an early period of fetal life the mesonephros—later the metanephros, or permanent kidney—becomes functional and excretes urea, etc., which finds its way out of the cloaca or of the bladder and enters the amniotic fluid. The amniotic fluid—as stated above—may be swallowed by the fetus during the later stages of intrauterine life. This accounts for the presence of urea in the alimentary tract of the newborn.

FIG. 337



The human mammary gland. (Kirke.)

b. Motosensory Activity.

That the fetus is conscious of any sensation is not even remotely probable. That the fetus responds reflexly to various stimuli is beyond question. The "quickening," which takes place at the middle of the period of intrauterine life, is the beginning of general body movements. From the first quickening to within about a week of delivery the movements increase in frequency, strength, and evident reflex character.

9. THE PHYSIOLOGY OF MATERNITY.

a. Pregnancy and Parturition.[1]

b. Lactation.

The milk-secreting glands are cutaneous, and the glandular epithelium is epiblastic in origin. The accompanying figure gives the most important anatomic features of the mammary gland (Fig. 337).

Fig. 338

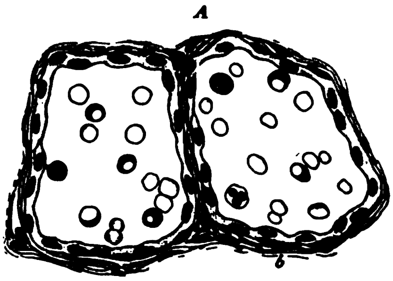
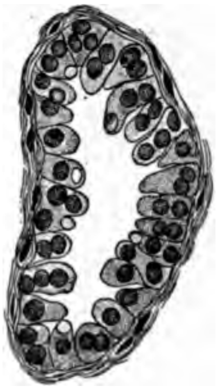
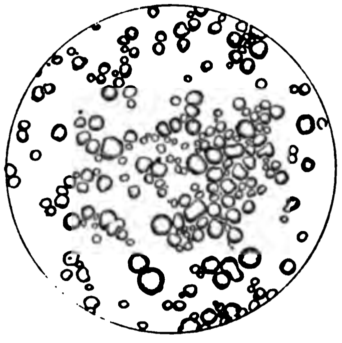


Fig. 339



Alveoli of the mammary gland of the bitch under different conditions of activity: *A*, section through the middle of two alveoli at the commencement of lactation, the epithelial cells being seen in profile; *B*, an alveoli in full secretory activity: (Schäfer, after Heidenhain.)

Fig. 340



Globules of cows' milk. × 400. (Kirke.)

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[1] These topics, though properly in the field of physiology, are extensively discussed in works on obstetrics. They need not be taken up here.

The secretion of the milk is analogous to the secretion of the oil of oil glands, in that the cellular elements of the gland epithelium are sacrificed in the process. Figs. 338 and 339 show the glandular alveoli under different stages of activity.

Milk has, under the microscope, the appearance shown in Fig. 340. The corpuscular elements are either colostrum corpuscles or casein-pellicled oil globules.

Milk is a physiologic emulsion and has the chemical constitution shown in the following table:

COMPOSITION OF HUMAN MILK.

Water	902.717
Casein (desiccated)	29.000
Lactoprotein	1.000
Albumin	......
Butter	25.000
Sugar of milk	37.000
Sodium lactate	0.420
Sodium chloride	0.240
Potassium chloride	1.440
Sodium carbonate	0.053
Calcium carbonate	0.069
Calcium phosphate	2.310
Magnesium phosphate	0.420
Sodium phosphate	0.225
Ferric phosphate	0.032
Sodium sulphate	0.074
Potassium sulphate	......
	1000.000

Gases in solution	Oxygen	1.29	30 parts per 1000 in volume.
	Nitrogen	12.17	
	Carbonic acid	16.54	

Milk contains food for the teeth and food for the bones, food for the muscles and food for the nervous system. It is a perfect food, satisfying every need of the developing infant.

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